L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:276008 CAPLUS
DOCUMENT NUMBER: 136:310071
TITLE: Preparation of bile-acid derived compounds for sustained release of orally delivered drugs
INVENTOR(S): Gallop, Mark A.; Cundy, Kenneth C.; Zhou, Cindy X.
PATENT ASSIGNEE(S): Xenoport, Inc., USA
SOURCE: PCT Int. Appl., 214 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028881	A1	20020411	WO 2001-US42513	20011005
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002011863	A5	20020415	AU 2002-11863	20011005
US 2002151529	A1	20021017	US 2001-972425	20011005

PRIORITY APPLN. INFO.: US 2000-238758P P 20001006
US 2000-249804P P 20001117
US 2001-297594P P 20010611
WO 2001-US42513 W 20011005

OTHER SOURCE(S): MARPAT 136:310071

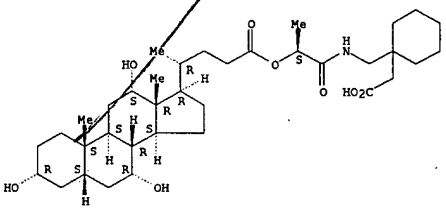
AB Bile-acid conjugates such as I [R1, R2 = H, OH; X = OH, DQT; T = O, NH; Q = bond, cleavable linker; D = GABA analog; Z = alkyl substituted with CO2H, SO3H, SO2H, P(O)(OR6)(OH), OSO3H; R6 = (un)substituted alkyl, aryl; MQ'D'; M = CH2OC(O), CH2CH2C(O); Q' = bond, cleavable linker; D' = D], or their pharmaceutically acceptable salts, were prepd. for their use as substrates for an intestinal bile acid transporter, and thus I could be utilized to provides sustained systemic concns. of orally delivered drugs to an animal. Thus, prodrug II was prepd. via treatment of the acid with NaOH obtained by the reaction of cholic acid and 1-aminomethyl-1-cyclohexaneacetic acid hydrochloride. Prodrug II was pharmacol. tested [IC50 = 36 .mu.M vs. IBAT-expressing cells; IC50 = 8 .mu.M vs. LBAT-expressing cells].

IT **410076-39-0P 410076-41-4P 410076-43-6P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of bile-acid derived compds. for providing sustained systemic concns. of drugs after oral administration)

RN 410076-39-0 CAPLUS
CN Cholan-24-oic acid, 3,7,12-trihydroxy-, 2-[[[1-(carboxymethyl)cyclohexyl]methyl]amino]-2-oxoethyl ester, (3.alpha.,5.beta.,7.alpha.,12.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS (Continued)



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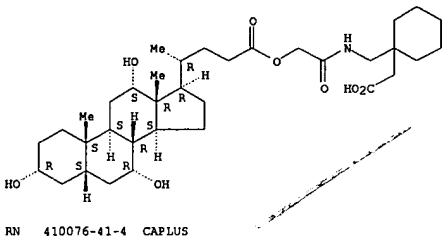
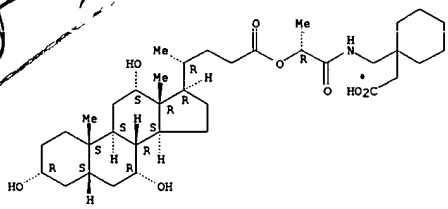
L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS (Continued)



RN 410076-41-4 CAPLUS
CN Cholan-24-oic acid, 3,7,12-trihydroxy-, (1R)-2-[[[1-(carboxymethyl)cyclohexyl]methyl]amino]-1-methyl-2-oxoethyl ester, (3.alpha.,5.beta.,7.alpha.,12.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 410076-43-6 CAPLUS
CN Cholan-24-oic acid, 3,7,12-trihydroxy-, (1S)-2-[[[1-(carboxymethyl)cyclohexyl]methyl]amino]-1-methyl-2-oxoethyl ester, (3.alpha.,5.beta.,7.alpha.,12.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

=> d ibib ab fqhit

L8 ANSWER 1 OF 1 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 137:20509 MARPAT
TITLE: Preparation and formulation of bile-acid derived compounds for enhancing oral absorption and systemic bioavailability of drugs
INVENTOR(S): Gallop, Mark A.; Cundy, Kenneth C.
PATENT ASSIGNEE(S): Xenoport, Inc., USA
SOURCE: PCT Int. Appl., 185 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002044324	A2	20020606	WO 2001-US42612	20011005
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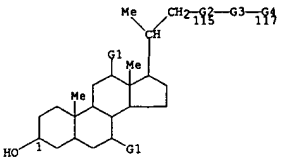
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002043204	A5	20020611	AU 2002-43204	20011005
US 2002099041	A1	20020725	US 2001-972411	20011005
PRIORITY APPLN. INFO.:			US 2000-238758P	20001006
			WO 2001-US42612	20011005

AB Bile acid derived prodrugs of the form D-Y-T [D = a drug which is incompletely translocated across the intestinal wall; Y = cleavable linking group; T = a bile acid moiety to permit the prodrug to be translocated across the intestinal wall via the bile acid transport system] were prepd. for pharmaceutical use. Thus, bile acid conjugate I was prepd. starting from cholic acid, glycine tert-Bu ester, succinic anhydride, BrCH2Cl, and cefmetazole sodium salt. The prepd. bile acid derived prodrugs were assayed in vitro for compd. transport with IBAT and NTCP expressing cell lines. Disclosed are methods for providing enhanced systemic blood concns. of orally delivered drugs that are incompletely translocated across the intestinal wall of an animal. Also disclosed are methods for the sustained release of drugs, whether poorly or readily bioavailable via oral delivery to animals. Still further, disclosed are compds. and pharmaceutical compns. that are used in such methods.

MSTR 2



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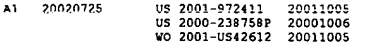
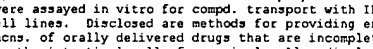
G3 = 125-115 129-117



G5 = CO2H
G9 = NH (SO) / O
G10 = Ak<EC (1-) C, BD (0-) D (0-) T> (SO G5)
G11 = C(O)
G12 = (0-2) 130-127 131-129



G14 = Ak<EC (1-) C, BD (0-) D (0-) T> (SO)
MPL: claim 20
NTE: and pharmaceutically acceptable salts
NTE: additional ring formation also claimed

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=> d his

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L27             STRUCTURE UPLOADED
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=> d ibib ab hitstr 1-40

L6 ANSWER 1 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:869795 CAPLUS
DOCUMENT NUMBER: 138:181158
TITLE: Absorption of biologically active peptide hormones from the small intestine of rat
AUTHOR(S): Wheeler, S.; McGinn, B. J.; Lucas, M. L.; Morrison, J. D.
CORPORATE SOURCE: University of Glasgow, Glasgow, G12 8QQ, UK
SOURCE: Acta Physiologica Scandinavica (2002), 176(3), 203-213
CODEN: APSCAX; ISSN: 0001-6772
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Absorption of the 4, 10 and 34 amino acid forms of gastrin from the small intestine has been investigated in anesthetized rats. The method of assessment of successful absorption of the hormone into the systemic circulation was when the amt. of acid secreted by the stomach over consecutive 15-min periods was increased. When the natural hormones were infused into the ileum in a relatively high dose, there was no increase in gastric acid secretion, indicating that they had not been absorbed. Each of the forms of gastrin was conjugated at the free N-terminus to the carboxyl group of cholic acid. Subsequent infusion of the conjugated form of gastrin into the ileum, this time in relatively low doses, resulted in substantial and prolonged increases in gastric acid secretion, indicating that these hormones had been successfully absorbed. In addn., conjugation of the 10 and 34 amino acid forms of gastrin with cholic acid was shown to increase markedly the potency in evoking an increase in gastric acid secretion in response to i.v. injection of the hormone. Absorption of the gastrin conjugates was specific to the ileum thus indicating that they had been absorbed through the bile salt transporters.

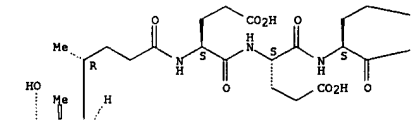
IT **324753-46-0**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(absorption of biol. active peptide hormones from the small intestine of rat)

RN 324753-46-0 CAPLUS
CN L-Phenylalaninamide, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-alanyl-L-tyrosylglycyl-L-tryptophyl-L-methionyl-L-.alpha.-asparty- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 1 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-A



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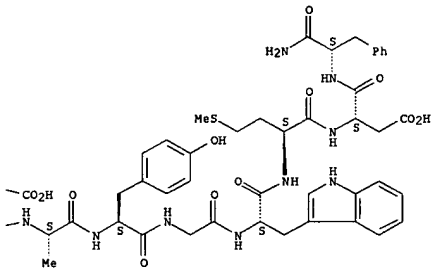

L6 ANSWER 1 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

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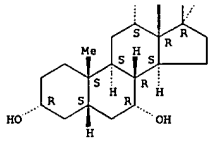


REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:849663 CAPLUS
DOCUMENT NUMBER: 137:353216
TITLE: Preparation of bile acid derivatives and their therapeutic use
INVENTOR(S): Faarup, Peter
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002088166	A1	20021107	WO 2002-DK250	20020418
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002183531	A1	20021205	US 2002-141469	20020501
PRIORITY APPLN. INFO.:			DK 2001-688 A	20010502
			US 2001-297388P P	20010611

OTHER SOURCE(S): CASREACT 137:353216

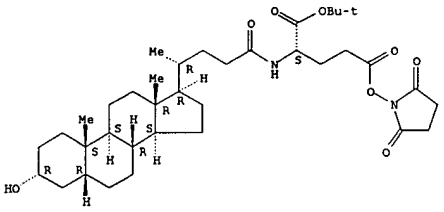
AB Certain bile acids find use in the pharmaceutical industry. In view of the wide distribution of serious diseases, such as HIV, AIDS and Bovine Spongiform Encephalopathy (BSE), it is desirable to avoid - as far as practicable - to have any components of animal origin in medicaments in order to eliminate any danger of infection. The present invention relates to a method of providing bile acids from non-animal starting materials. Thus, lithocholic acid was prepd. via a multistep reaction sequence starting from stigmasterol obtained from soy beans.

IT **240133-29-3 474327-44-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of lithocholic acid from stigmasterol obtained from soy beans)

RN 240133-29-3 CAPLUS
CN L-Norvaline, 5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-N-[(3.alpha.,5.beta.)-3-hydroxy-24-oxocholan-24-yl]-5-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

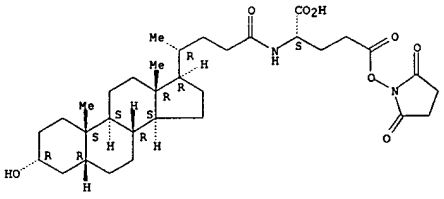
Absolute stereochemistry.

L6 ANSWER 2 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 474327-44-1 CAPLUS
CN L-Norvaline, 5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-N-[(3.alpha.,5.beta.)-3-hydroxy-24-oxocholan-24-yl]-5-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:796661 CAPLUS
DOCUMENT NUMBER: 138:21182
TITLE: Ion Conductors Derived from Biogenic Amines, Bile Acids, and Amino Acids
AUTHOR(S): Bandyopadhyay, Punam; Bandyopadhyay, Prasun; Regen, Steven L.
CORPORATE SOURCE: Department of Chemistry, Lehigh University, Bethlehem, PA, 18015, USA
SOURCE: Bioconjugate Chemistry (2002), 13(6), 1314-1318
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A family of conjugates has been synthesized from spermine, putrescine, lysine, .gamma.-aminobutyric acid, sarcosine, cholic acid, glycocholic acid, 3.alpha.,7.alpha.-dihydroxycholic acid, and 3.alpha.,12.alpha.-dihydroxycholic acid, based on a design principle previously reported (Bandyopadhyay, P., Janout, V., Zhang, L., Regen, S. L. (2001) J. Am. Chem. Soc. 123, 7691). Each of these conjugates was found to exhibit significant activity in promoting the transport of Na+ across liposomal membranes derived from 1,2-dimyristoleoyl-sn-glycero-3-phosphocholine, and also from 1,2-dipalmitoleoyl-sn-glycero-3-phosphocholine. In all cases, plots of pseudo first-order rate consts., kobsd vs (mol % of ion conductor)2 were found to be linear, indicating that transport-active dimers are involved and that only a small fraction of the conjugates are in an aggregated form. An operational comparison that has been made within this series of conjugates indicates that Na+ transport activity and membrane selectivity have a moderate dependency on the compn. and the structure of the ion conductor.

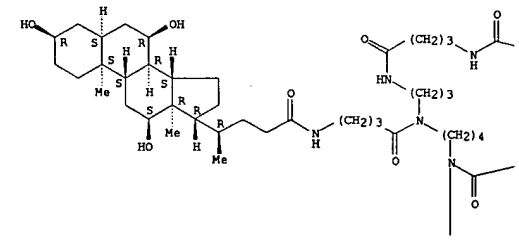
IT **478182-21-7P**
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(sodium cation transport activity and membrane selectivity have moderate dependency on compn. and structure of ion conductor derived from biogenic amines, bile acids, and amino acids)

RN 478182-21-7 CAPLUS
CN Cholan-24-amide, N,N'-[4,19-dioxo-9,14-bis[1-oxo-4-[[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]pentyl]-5,9,14,18-tetrazadocosane-1,22-diyl]bis[3,7,12-trihydroxy-, (3.alpha.,5.beta.,7.alpha.,12.alpha.)-(3'.alpha.,5'.beta.,7'.alpha.,12'.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 3 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-A



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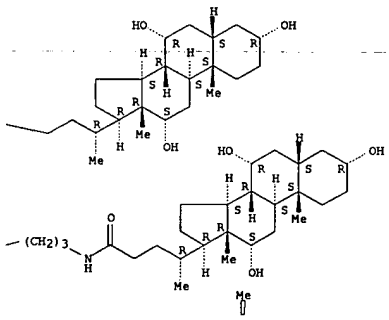

L6 ANSWER 3 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

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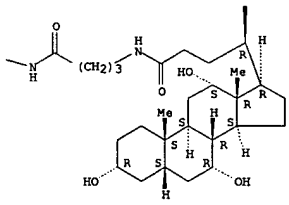
PAGE 2-B



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:314729 CAPLUS
DOCUMENT NUMBER: 136:330526
TITLE: Bile-acid conjugates for providing sustained systemic concentrations of drugs
INVENTOR(S): Gallop, Mark A.; Cundy, Kenneth C.; Zhou, Cindy X.
PATENT ASSIGNEE(S): Xenoport, Inc., USA
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032376	A2	20020425	WO 2001-US42613	20011005
WO 2002032376	A3	20030904		
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AU 2002030398	A5	20020429	AU 2002-30398	20011005
US 2002111338	A1	20020815	US 2001-972283	20011005
US 2002142998	A1	20021003	US 2001-974768	20011009

PRIORITY APPLN. INFO.: US 2000-238758P P 20001006
US 2000-249804P P 20001117
US 2001-297472P P 20010611
WO 2001-US42613 W 20011005

OTHER SOURCE(S): MARPAT 136:330526

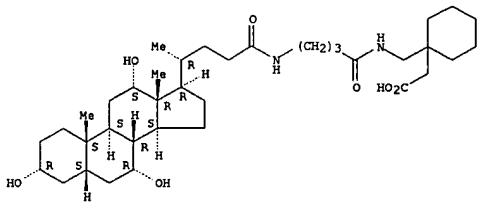
AB This invention is directed to compds. that provide for sustained systemic concns. of therapeutic or prophylactic agents following administration to animals. This invention is also directed to pharmaceutical compns. including and methods using such compds. Among example compds. prepd. was I. Examples were give for in vitro transport for the compds. of IBAT (Na-dependent transporter)-expressing cells.

IT **406936-53-6P 413597-16-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bile-acid conjugates for providing sustained systemic concns. of drugs)

RN 406936-53-6 CAPLUS
CN Cyclohexaneacetic acid, 1-[[[(1S)-1-oxo-4-[[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]butyl]amino]methyl]- (9CI) (CA INDEX NAME)

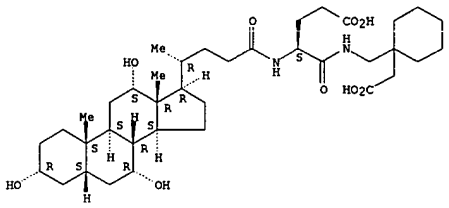
Absolute stereochemistry.

L6 ANSWER 4 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 413597-16-7 CAPLUS
CN Cyclohexaneacetic acid, 1-[[[(1S)-4-carboxy-1-oxo-2-[[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]butyl]amino]methyl]-, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● Na

L6 ANSWER 5 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:276010 CAPLUS
DOCUMENT NUMBER: 136:294977
TITLE: Preparation of bile acid conjugates for providing sustained systemic concentrations of drugs
INVENTOR(S): Gallop, Mark A.; Cundy, Kenneth C.
PATENT ASSIGNEE(S): Xenoport, Inc., USA
SOURCE: PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028883	A1	20020411	WO 2001-US42628	20011009
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002111338	A1	20020815	US 2001-972283	20011005
AU 2002013468	A5	20020415	AU 2002-13468	20011009
US 2002142998	A1	20021003	US 2001-974768	20011009

PRIORITY APPLN. INFO.: US 2000-238758P P 20001006
US 2000-249804P P 20001117
US 2001-297472P P 20010611
WO 2001-US42628 W 20011009

OTHER SOURCE(S): MARPAT 136:294977

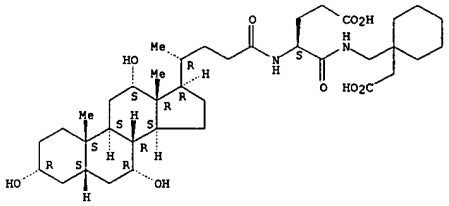
AB Bile acid conjugates, such as I [R1, R2 = H, OH; R3 = amide linked amino acid or peptide moiety], were prepd. for pharmaceutical use as drug delivery moieties which provide for sustained systemic concns. of drugs. Thus, cholyl-Gly-Gabapentin II (R = H) was prepd. by amide formation of cholic acid with glycine using ClCO2Et and Et3N in THF and subsequent amide formation of the glycine cholic acid amide with gabapentin using the same reagents. The prepd. bile acid conjugates underwent in vitro compd. transport assays with IBAT and LBAT expressing cell lines for inhibition of radiolabeled taurocholate uptake and assays with PEPT1 and PEPT2 expressing cells lines for inhibition of radiolabeled Gly-Sar uptake. Also, enzymic releaas of gabapentin for the conjugates by pancreatin and pharmacokinetics of the prodrug cholyl-Phe-Gabapentin II (R = CH2Ph) were examd.

IT **406936-49-0P 406936-53-6P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of bile acid conjugates for providing sustained systemic concns. of drugs)

RN 406936-49-0 CAPLUS
CN Cyclohexaneacetic acid, 1-[[[(1S)-4-carboxy-1-oxo-2-[[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]butyl]amino]methyl]- (9CI) (CA INDEX NAME)

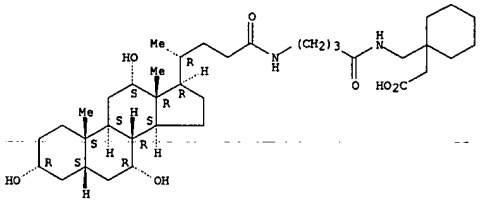
Absolute stereochemistry.

L6 ANSWER 5 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 406936-53-6 CAPLUS
CN Cyclohexaneacetic acid, 1-[[[(1S)-1-oxo-4-[[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]butyl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:276008 CAPLUS
DOCUMENT NUMBER: 136:310071
TITLE: Preparation of bile-acid derived compounds for sustained release of orally delivered drugs
INVENTOR(S): Gallop, Mark A.; Cundy, Kenneth C.; Zhou, Cindy X.
PATENT ASSIGNEE(S): Xenoport, Inc., USA
SOURCE: PCT Int. Appl., 214 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028881	A1	20020411	WO 2001-US42513	20011005
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002011863	A5	20020415	AU 2002-11863	20011005
US 2002151529	A1	20021017	US 2001-972425	20011005
EP 1343805	A1	20030917	EP 2001-979953	20011005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-238758P P 20001006
US 2000-249804P P 20001117
US 2001-297594P P 20010611
WO 2001-US42513 W 20011005

OTHER SOURCE(S): MARPAT 136:310071

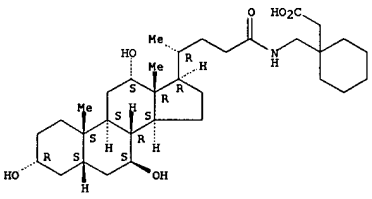
AB Bile-acid conjugates such as I [R1, R2 = H, OH; X = OH, DQT; T = O, NH; Q = bond, cleavable linker; D = GABA analog; Z = alkyl substituted with CO2H, SO3H, SO2H, P(O)(OR6)(OH), OSO3H; R6 = (un)substituted alkyl, aryl, MQ'D'; M = CH2OC(O), CH2CH2C(O); Q' = bond, cleavable linker; D' = D], or their pharmaceutically acceptable salts, were prepd. for their use as substrates for an intestinal bile acid transporter, and thus I could be utilized to provides sustained systemic concns. of orally delivered drugs to an animal. Thus, prodrug II was prepd. via treatment of the acid with NaOH obtained by the reaction of cholic acid and 1-aminomethyl-1-cyclohexaneacetic acid hydrochloride. Prodrug II was pharmacol. tested [IC50 = 36 .mu.M vs. IBAT-expressing cells; IC50 = 8 .mu.M vs. LBAT-expressing cells].

IT **406936-20-7P**, XP 10569 **410076-19-6P 410076-45-8P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of bile-acid derived compds. for providing sustained systemic concns. of drugs after oral administration)

RN 406936-20-7 CAPLUS
CN Cyclohexaneacetic acid, 1-[[[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]methyl]-, monosodium salt (9CI) (CA INDEX NAME)

L6 ANSWER 6 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

Absolute stereochemistry.

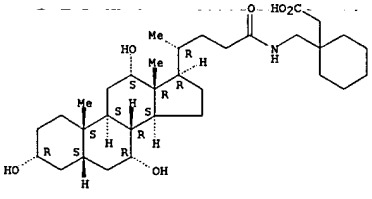


● Na

IT **406936-19-4P 410076-29-8P 410076-44-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of bile-acid derived compds. for providing sustained systemic concns. of drugs after oral administration)

RN 406936-19-4 CAPLUS
CN Cyclohexaneacetic acid, 1-[[[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

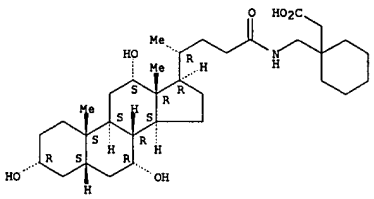


RN 410076-29-8 CAPLUS
CN L-Glutamic acid, N-[(3.alpha.,5.beta.,7.alpha.,12.beta.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-, 1-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 6 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
INDEX NAME)

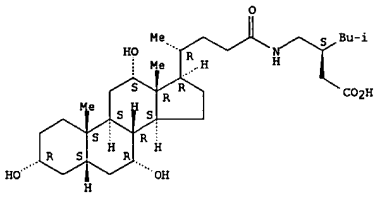
Absolute stereochemistry.



● Na

RN 410076-19-6 CAPLUS
CN Hexanoic acid, 5-methyl-3-[[[(3.alpha.,5.beta.,7.alpha.,12.beta.)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]methyl]-, monosodium salt, (3S)- (9CI) (CA INDEX NAME)

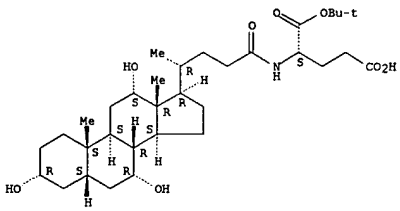
Absolute stereochemistry.



● Na

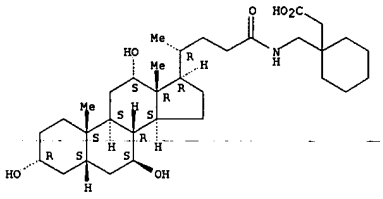
RN 410076-45-8 CAPLUS
CN Cyclohexaneacetic acid, 1-[[[(3.alpha.,5.beta.,7.beta.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]methyl]-, monosodium salt (9CI) (CA INDEX NAME)

L6 ANSWER 6 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 410076-44-7 CAPLUS
CN Cyclohexaneacetic acid, 1-[[[(3.alpha.,5.beta.,7.beta.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:275808 CAPLUS
DOCUMENT NUMBER: 136:295094
TITLE: Preparation of compounds for sustained release of orally delivered drugs
INVENTOR(S): Gallop, Mark A.; Cundy, Kenneth C.
PATENT ASSIGNEE(S): Xenoport, Inc., USA
SOURCE: PCT Int. Appl., 151 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028411	A1	20020411	WO 2001-US31486	20011005
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002011538	A5	20020415	AU 2002-11538	20011005
US 2002098999	A1	20020725	US 2001-972402	20011005
EP 1343515	A1	20030917	EP 2001-979594	20011005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

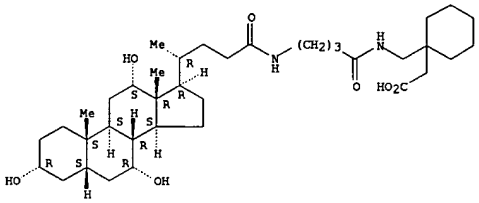
PRIORITY APPLN. INFO.:
US 2000-238758P A1 20001006
US 2000-249804P P 20001117
US 2001-297594P P 20010611
US 2001-297641P P 20010611
US 2001-297654P P 20010611
WO 2001-US31486 W 20011005

AB Disclosed are compds. and pharmaceutical compns. that are used for providing sustained systemic blood concns. of orally delivered drugs. Comounds D-Y-T [D is a drug having therapeutic or prophylactic activity when delivered to the systemic circulation of said animal; T is a moiety selected to permit the compd. D-Y-T or an active metabolite to be translocated across the intestinal wall of an animal and participate in the enterohepatic circulation in said animal; and Y is a cleavable linker covalently connecting D to T, where Y is selected such that a portion of the linker is cleaved to release drug D or an active metabolite during each cycle through the enterohepatic circulation whereupon sustained release of drug D in said animal is achieved] are claimed. Thus, a series of cholyl-amino acid-gabapentin prodrugs was prepd. and the in vitro enzymic release of gabapentin evaluated.

IT **406936-20-7P 406936-49-0P 406936-53-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of compds. for sustained release of orally delivered drugs)

RN 406936-20-7 CAPLUS
CN Cyclohexaneacetic acid, 1-[[[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-

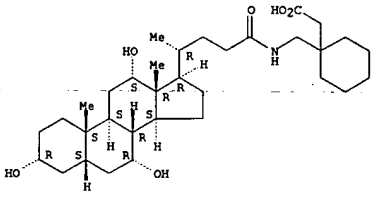
L6 ANSWER 7 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



IT **406936-19-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of compds. for sustained release of orally delivered drugs)

RN 406936-19-4 CAPLUS
CN Cyclohexaneacetic acid, 1-[[[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]methyl]- (9CI) (CA INDEX NAME)

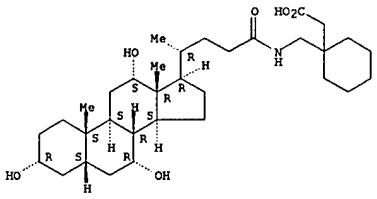
Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
trihydroxy-24-oxocholan-24-yl]amino]methyl]-, monosodium salt (9CI) (CA INDEX NAME)

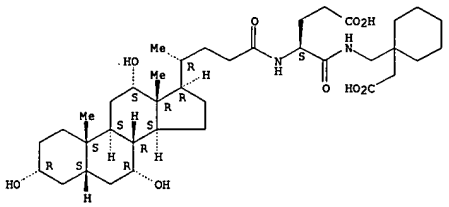
Absolute stereochemistry.



● Na

RN 406936-49-0 CAPLUS
CN Cyclohexaneacetic acid, 1-[[[(1S)-4-carboxy-1-oxo-2-[[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]butyl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 406936-53-6 CAPLUS
CN Cyclohexaneacetic acid, 1-[[[(1S)-1-oxo-4-[[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]butyl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 8 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:886239 CAPLUS
DOCUMENT NUMBER: 136:37953
TITLE: Glucose dependent release of insulin from glucose sensing insulin derivatives
INVENTOR(S): Jensen, Thomas Hoeg; Havelund, Svend; Markussen, Jan; Ostergaard, Soren; Ridderberg, Signe; Balschmidt, Per; Schaeffer, Lauge; Jonassen, Ib
PATENT ASSIGNEE(S): Novo Nordisk A/s, Den.
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001092334	A1	20011206	WO 2001-DK382	20010601
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002028767	A1	20020307	US 2001-870884	20010531
EP 1290024	A1	20030312	EP 2001-938005	20010601
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.:
DK 2000-858 A 20000602
US 2000-213375P P 20000623
WO 2001-DK382 W 20010601

OTHER SOURCE(S): MARPAT 136:37953

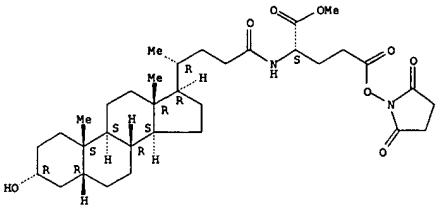
AB The invention relates to insulin derivs. having a built-in glucose sensor, capable of delivering insulin from a depot as a function of the glucose concn. in the surrounding medium (e.g., tissue). Thus, LysB29[N.epsilon.-(.gamma.-glutamyl-N.alpha.-lithocholoyl)],LysB30(N.epsilon.-3-nitro-5-boronobenzoyl)human insulin (17) was prepd. by coupling N.epsilon.-(3-nitro-5-pinacolboronobenzoyl) Me lysinate hydrochloride (prepn. given) to the carboxylic acid group of LysB29 in des(B30) human insulin using achromobacter lyticus protease, acylation of the intermediate with .gamma.-hydroxysuccinimidyl .alpha.-Me glutamyl-N.alpha.-lithocholate, and sapon. Product 17 showed EC50 = 0.16 nM for binding to the insulin receptor and the intermediate in its synthesis showed EC50 = 16.1 nM for carbohydrate binding.

IT **377780-60-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(glucose dependent release of insulin from glucose sensing insulin derivs.)

RN 377780-60-4 CAPLUS
CN L-Norvaline, 5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-N-[(3.alpha.,5.beta.)-3-hydroxy-24-oxocholan-24-yl]-5-oxo-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 8 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:721487 CAPLUS
DOCUMENT NUMBER: 135:273221
TITLE: Preparation of lipophilic human glucagon-like peptide-1 derivatives with protracted action profiles
INVENTOR(S): Knudsen, Liselotte; Huusfeldt, Per Olaf; Nielsen, Per Franklin; Kaarsholm, Niels C.; Olsen, Helle Birk; Bjorn, Soren Erik; Pedersen, Freddy Zimmerdahl; Madsen, Kjeld
PATENT ASSIGNEE(S): Novo Nordisk A/s, Den.
SOURCE: U.S., 136 pp., Cont.-in-part of U.S. Ser. No. 38,432, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6268343	B1	20010731	US 1999-258750	19990226
WO 9808871	A1	19980305	WO 1997-DK340	19970822
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 2001011095	A2	20010116	JP 2000-152778	19970822
ZA 9707791	A	19980302	ZA 1997-7791	19970829
ZA 9707828	A	19980302	ZA 1997-7828	19970901
ZA 9901571	A	19990902	ZA 1999-1571	19990226
US 2001011071	A1	20010802	US 1999-398111	19990916
US 6458924	B2	20021001		
US 2002025933	A1	20020228	US 2001-908534	20010718

PRIORITY APPLN. INFO.:

DK 1996-931	A	19960830
DK 1996-1259	A	19961108
DK 1996-1470	A	19961220
US 1997-36255P	P	19970124
US 1997-36226P	P	19970125
WO 1997-DK340	A2	19970822
US 1997-918810	B2	19970826
DK 1998-263	A	19980227
DK 1998-264	A	19980227
DK 1998-268	A	19980227
DK 1998-272	A	19980227
DK 1998-274	A	19980227
US 1998-38432	B2	19980311
DK 1998-508	A	19980408
DK 1998-509	A	19980408
US 1998-82478P	P	19980421
US 1998-82480P	P	19980421
US 1998-84357P	P	19980421
US 1998-82802P	P	19980423
US 1997-35905P	P	19970124

L6 ANSWER 9 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

JP 1998-511183	A3	19970822
US 1997-922200	B2	19970902
DK 1998-271	A	19980227
US 1998-78422P	P	19980318
US 1998-82479P	P	19980421
US 1998-85789P	P	19980518
US 1999-258187	B1	19990225
US 1999-258750	A2	19990226
US 1999-265141	A2	19990308

OTHER SOURCE(S): MARPAT 135:273221

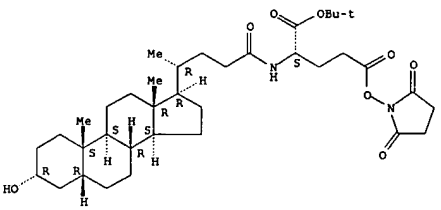
AB The present invention relates to human glucagon-like peptide-1 (GLP-1) derivs. having a lipophilic substituent, compns. contg. these derivs., and to methods for their prepn. A claimed compd. is His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Arg-Gly-Arg-Gly. Thus, coupling of GLP-1(7-37)-OH with Me(CH2)12CO-Glu(OSu)-OCMe3 (Su = succinimidyl) (prepn. given), followed by deesterification with CF3CO2H and chromatog. purifn. gave 8% bis-adduct Lys[Me(CH2)12CO-.gamma.-Glu]26,34-GLP-1(7-37)-OH. Several prepd. lipophilic GLP-1 analogs were tested for protracted plasma concn. in pigs and were found to be much more persistent than GLP-1(7-37). In addn., the time of peak plasma concn. was found to vary within wide limits depending on the particular lipophilic GLP-1 deriv. selected. The efficacy of several prepd. derivs. was tested by stimulation of cAMP in a cell line expressing cloned human GLP-1 receptor.

IT **240133-29-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(glucagon-like peptide conjugates; prepn. of lipophilic human glucagon-like peptide-1 derivs. with protracted action profiles)

RN 240133-29-3 CAPLUS

CN L-Norvaline, 5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-N-[(3.alpha.,5.beta.)-3-hydroxy-24-oxocholan-24-yl]-5-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:566665 CAPLUS
DOCUMENT NUMBER: 135:122756
TITLE: Preparation of lipophilic human glucagon-like peptide-1 derivatives with protracted action profiles
INVENTOR(S): Knudsen, Liselotte Bjerre; Huusfeldt, Per Olaf; Nielsen, Per Franklin; Kaarsholm, Niels C.; Olsen, Helle Birk; Bjorn, Soren Erik; Pedersen, Freddy Zimmerdahl; Madsen, Kjeld
PATENT ASSIGNEE(S): Den.
SOURCE: U.S. Pat. Appl. Publ., 133 pp., Cont.-in-part of U.S. Ser. No. 265,141.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001011071	A1	20010802	US 1999-398111	19990916
US 6458924	B2	20021001		
WO 9808871	A1	19980305	WO 1997-DK340	19970822
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 2001011095	A2	20010116	JP 2000-152778	19970822
ZA 9707791	A	19980302	ZA 1997-7791	19970829
ZA 9707828	A	19980302	ZA 1997-7828	19970901
US 6268343	B1	20010731	US 1999-258750	19990226
US 6384016	B1	20020507	US 1999-265141	19990308
US 2002025933	A1	20020228	US 2001-908534	20010718

PRIORITY APPLN. INFO.:

DK 1996-931	A	19960830
DK 1996-1259	A	19961108
DK 1996-1470	A	19961220
US 1997-36255P	P	19970124
US 1997-36226P	P	19970125
US 1998-84357P	P	19970822
WO 1997-DK340	W	19970822
US 1997-918810	B2	19970826
DK 1998-263	A	19980227
DK 1998-264	A	19980227
DK 1998-268	A	19980227
US 1998-38432	B2	19980311
US 1998-78422P	P	19980318
US 1998-82478P	P	19980421
US 1998-82479P	P	19980421
US 1998-82480P	P	19980421
US 1998-82802P	P	19980423
US 1999-258750	A2	19990226
US 1999-265141	A2	19990308
US 1997-35905P	P	19970124
JP 1998-511183	A3	19970822
US 1997-922200	B2	19970902
DK 1998-271	A	19980227
DK 1998-272	A	19980227

L6 ANSWER 10 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

	DK 1998-274	A	19980227
	EP 1998-610006	A	19980313
	DK 1998-508	A	19980408
	DK 1998-509	A	19980408
	US 1998-85789P	P	19980518
	US 1999-258187	B1	19990225

OTHER SOURCE(S): MARPAT 135:122756

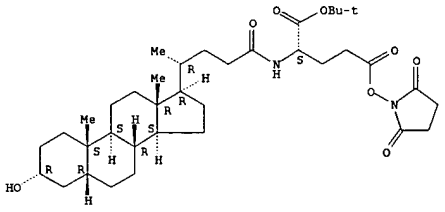
AB The present invention relates to pharmaceutical compns. comprising lipophilic human glucagon-like peptide-1 (GLP-1) derivs. having a lipophilic substituent and a surfactant. Thus, coupling of GLP-1(7-37)-OH with Me(CH2)12CO-Glu(OSu)-OCMe3 (Su = succinimidyl) (prepn. given), followed by deesterification with CF3CO2H and chromatog. purifn. gave 8% bis-adduct Lys[Me(CH2)12CO-.gamma.-Glu]26,34-GLP-1(7-37)-OH. Several prepd. lipophilic GLP-1 analogs were tested for protracted plasma concn. in pigs and were found to be much more persistent than GLP-1(7-37). In addn., the time of peak plasma concn. was found to vary within wide limits depending on the particular lipophilic GLP-1 deriv. selected. The efficacy of several prepd. derivs. was tested by stimulation of cAMP in a cell line expressing cloned human GLP-1 receptor.

IT **240133-29-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(glucagon-like peptide conjugates; prepn. of lipophilic human glucagon-like peptide-1 derivs. with protracted action profiles)

RN 240133-29-3 CAPLUS

CN L-Norvaline, 5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-N-[(3.alpha.,5.beta.)-3-hydroxy-24-oxocholan-24-yl]-5-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 11 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:101167 CAPLUS
DOCUMENT NUMBER: 134:168315
TITLE: Enhancement of bioavailability of peptides with bile salts
INVENTOR(S): Morrison, James Duncan; Lucas, Michael Leslie; Wheeler, Sarah
PATENT ASSIGNEE(S): The University Court of the University of Glasgow, UK
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 20010091 63	A2	20010208	WO 2000-GB2903	20000728
WO 2001009163	A3	20010907		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
GB 2355009	A1	20010411	GB 1999-17793	19990730
AU 2000061739	A5	20010219	AU 2000-61739	20000728
EP 1228093	A2	20020807	EP 2000-948177	20000728
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: GB 1999-17793 A 19990730
WO 2000-GB2903 W 20000728

OTHER SOURCE(S): MARPAT 134:168315

AB The present invention relates to improving and/or increasing the bioavailability of a biol. active substance, such as a peptide. In particular the present invention relates to the conjugation of the biol. active substance to a bile acid. The conjugated biol. active substance is suitable particularly for oral or parental administration. Illeal administration of 600.mu.g/kg gastrin tetrapeptide conjugated to cholate resulted in a significant mean increase in gastric acid secretion of 1.84 .mu.mol over a 3 h collection period, while no increase in acid secretion was noticed by administration of tetragastrin alone or with sep. cholate.

IT **324753-46-0**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(enhancement of bioavailability of peptides with bile salts)

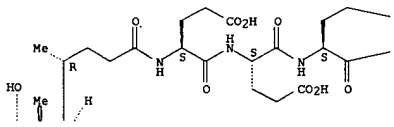
RN 324753-46-0 CAPLUS

CN L-Phenylalaninamide, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-alanyl-L-tyrosylglycyl-L-tryptophyl-L-methionyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 11 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-A



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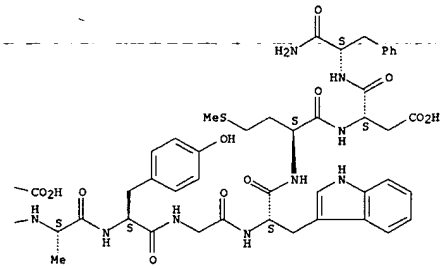
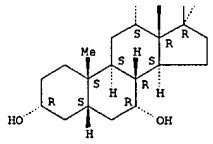


L6 ANSWER 11 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 2-A



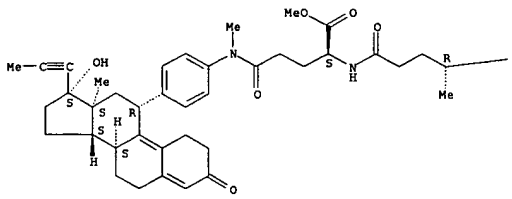
L6 ANSWER 12 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:707189 CAPLUS
DOCUMENT NUMBER: 133:267020
TITLE: synthesis and activity of liver specific bile acid derivatives of the glucocorticoid antagonist RU486
INVENTOR(S): Apelqvist, Theresa; Wu, Jinchang; Koehler, Konrad F.
PATENT ASSIGNEE(S): Karo Bio AB, Swed.
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000058337	A1	20001005	WO 2000-EP2429	20000318
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1165595	A1	20020102	EP 2000-922530	20000318
EP 1165595	B1	20030514		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002540215	T2	20021126	JP 2000-608037	20000318
AU 758654	B2	20030327	AU 2000-42893	20000318
AT 240346	E	20030515	AT 2000-922530	20000318
US 6468975	B1	20021022	US 2002-937374	20020211
PRIORITY APPLN. INFO.:			GB 1999-7048 A	19990327
			WO 2000-EP2429 W	20000318

OTHER SOURCE(S): MARPAT 133:267020
AB Novel glucocorticoid receptor ligands of formula (I) [R = H, aliph. hydrocarbon, arom. hydrocarbon, carboxylic acid or ester, alkenyl carboxylic acid or ester, hydroxy, halogen, cyano halogen, cyano; W = methine carbon having the R, S, or racemic stereochem; X and Z are the same or are different and = bond, amide (-CONR'- or -NR1CO-), amine (-NR'-), ether (-O-), or thioether (-S-) and R1 = H, aliph. hydrocarbon, or arom. hydrocarbon; n, o are the same or are different and = 1-6, m = 0-6; Y = hydroxyl group, carboxylic acid or ester, tetrazole, acylsulfonamide (-CONHSO2R2 or -SO2NHCOR2 where R2 = aliph. or arom. hydrocarbon)] or a pharmaceutically acceptable salt thereof are synthesized and tested. A method for treating diseases assocd. with metab. dysfunction or which are dependent on the expression of a glucocorticoid such as diabetes are claimed.
IT **298186-91-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and activity of liver specific bile acid derivs. of the glucocorticoid antagonist RU486)
RN 298186-91-1 CAPLUS

L6 ANSWER 12 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-A



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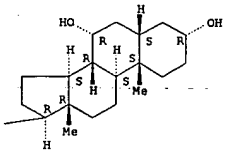
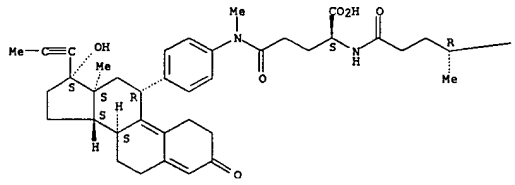


REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

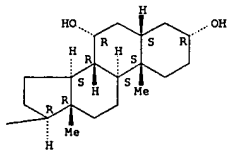
L6 ANSWER 12 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
CN L-Glutamine, N2-[(3.alpha.,5.beta.,7.alpha.)-3,7-dihydroxy-24-oxocholan-24-yl]-N-[4-[(11.beta.,17.beta.)-17-hydroxy-3-oxo-17-(1-propynyl)estra-4,9-dien-11-yl]phenyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT **298186-94-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and activity of liver specific bile acid derivs. of the glucocorticoid antagonist RU486)
RN 298186-94-4 CAPLUS
CN L-Glutamine, N2-[(3.alpha.,5.beta.,7.alpha.)-3,7-dihydroxy-24-oxocholan-24-yl]-N-[4-[(11.beta.,17.beta.)-17-hydroxy-3-oxo-17-(1-propynyl)estra-4,9-dien-11-yl]phenyl]-N-methyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

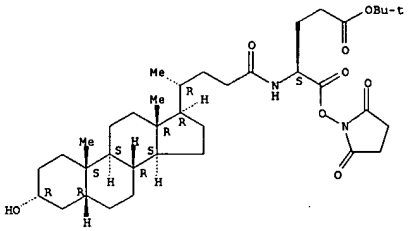
L6 ANSWER 13 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:10612 CAPLUS
DOCUMENT NUMBER: 132:73648
TITLE: Lipophilic insulin derivatives soluble at physiological pH with prolonged serum half-lives and biological activity
INVENTOR(S): Havelund, Svend; Halstrom, John; Jonassen, Ib; Andersen, Asser Sloth; Markussen, Jan
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: U.S., 47 pp., Cont.-in-part of U.S. 5,750,497.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6011007	A	20000104	US 1997-975365	19971120
ZA 9407187	A	19950317	ZA 1994-7187	19940916
JP 2000060556	A2	20000229	JP 1999-221632	19940916
EP 1132404	A2	20010912	EP 2001-112992	19940916
EP 1132404	A3	20020327		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT				
JP 2002308899	A2	20021023	JP 2001-385921	19940916
US 5750497	A	19980512	US 1995-400256	19950308
AU 745983	B2	20020411	AU 2000-51960	20000811
PRIORITY APPLN. INFO.:			DK 1993-1044 A	19930917
			US 1995-400256 A2	19950308
			US 1994-190829 A	19940202
			EP 1994-926816 A3	19940916
			JP 1995-508923 A3	19940916
			JP 1999-221632 A3	19940916

OTHER SOURCE(S): MARPAT 132:73648
AB Human insulin derivs. with improved soly. at physiol. pH and that retain biol. activity for longer than wild-type human insulin are described. The insulins are substituted at positions A21 and B3 with either being any amino acid except lysine, arginine, or cysteine. The phenylalanine at B1 may be deleted and the amino acid at position B30 may be deleted or substituted by any amino acid except lysine, arginine, or cysteine or by another amino acid that is lipophilic having a C10-24 side chain. If B30 is deleted or substituted, lysineB29 is modified by a carboxylic acid connected to the .epsilon.-amino group. When B30 is threonine or alanine and A21 and B3 are both asparagine, and phenylalanineB1 is present, then the insulin deriv. is always present as a Zn2 complex.
IT **168986-19-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation of insulin derivs. using; lipophilic insulin derivs. sol. at physiol. pH with prolonged serum half-lives and biol. activity)
RN 168986-19-4 CAPLUS
CN Pentanoic acid, 5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-[[(3.alpha.,5.beta.)-3-hydroxy-24-oxocholan-24-yl]amino]-5-oxo-, 1,1-dimethylethyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 13 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:566075 CAPLUS
DOCUMENT NUMBER: 131:200093
TITLE: Preparation of GLP-1 analogs for treatment of obesity and non-insulin dependent diabetes mellitus
INVENTOR(S): Knudsen, Liselotte Bjerre; Huusfeldt, Per Olaf; Nielsen, Per Franklin; Pedersen, Freddy Zimmerdahl
PATENT ASSIGNEE(S): Novo Nordisk A/s, Den.
SOURCE: PCT Int. Appl., 270 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943706	A1	19990902	WO 1999-DK82	19990225
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9926106	A1	19990915	AU 1999-26106	19990225
EP 1060191	A1	20001220	EP 1999-906076	19990225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, FI, RO				
ZA 9901569	A	19990827	ZA 1999-1569	19990226
ZA 9901570	A	19990902	ZA 1999-1570	19990226

PRIORITY APPLN. INFO.: DK 1998-268 A 19980227
WO 1999-DK82 W 19990225
OTHER SOURCE(S): MARPAT 131:200093

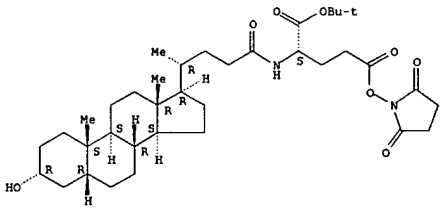
AB GLP-1 analog derivs. His-Xaa8-Xaa9-Gly-Xaa11-Phe-Thr-Xaa14-Asp-Xaa16-Xaa17-Xaa18-Xaa19-Xaa20-Xaa21-Xaa22-Xaa23-Xaa24-Xaa25-Xaa26-Xaa27-Phe-Ile-Xaa30-Xaa31-Xaa32-Xaa33-Xaa34-Xaa35-Xaa36-Xaa37-Xaa38-Xaa39-Xaa40-Xaa41-Xaa42-Xaa43-Xaa44-Xaa45 [Xaa represents an amino acid residue, e.g., Xaa8, Xaa25, Xaa30 = Ala, Gly, Ser, Thr, Leu, Ile, Val, Glu, Asp, Lys; Xaa9, Xaa21, Xaa27 = Glu, Asp, Lys; Xaa11 = Thr, Ala, Gly, Ser, Leu, Ile, Val, Glu, Asp, Lys; Xaa14, Xaa17, Xaa18 = Val, Ala, Gly, Ser, Thr, Leu, Ile, Tyr, Glu, Asp, Lys] having a lipophilic substituent were prepd. for the treatment of obesity and non-insulin dependent diabetes mellitus. Thus, Arg26-34,Lys36[N.epsilon.-[.gamma.-glutamyl(N.alpha.-hexadecanoyl)]] GLP-1 (7-36)-OH was prepd. via reaction of Arg26-34,Lys36 GLP-1 (7-36)-OH with Pal-Glu(ONSu)-But (Pal = hexadecanoyl, NSU = succinimide residue). The synthesized compds. have a protracted profile of action relative to GLP-1 (7-37).

IT **240133-29-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of GLP-1 analogs for treatment of obesity and non-insulin dependent diabetes mellitus)

RN 240133-29-3 CAPLUS
CN L-Norvaline, 5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-N-[(3.alpha.,5.beta.)-3-hydroxy-24-oxocholan-24-yl]-5-oxo-, 1,1-dimethylethyl ester (9CI) (CA

L6 ANSWER 14 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 15 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:565926 CAPLUS
DOCUMENT NUMBER: 131:185249
TITLE: GLP-1 derivatives with helix-content exceeding 25 %, forming partially structured micellar-like aggregates
INVENTOR(S): Knudsen, Liselotte Bjerre; Huusfeldt, Per Olaf; Nielsen, Per Franklin; Kaarsholm, Niels C.; Olsen, Helle Birk; Bjorn, Soren Erik
PATENT ASSIGNEE(S): Novo Nordisk A/s, Den.
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943341	A1	19990902	WO 1999-DK84	19990225
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9926107	A1	19990915	AU 1999-26107	19990225
EP 1061946	A1	20001227	EP 1999-906077	19990225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2002504518	T2	20020212	JP 2000-533137	19990225

PRIORITY APPLN. INFO.: DK 1998-268 A 19980227
DK 1998-272 A 19980227
WO 1999-DK84 W 19990225

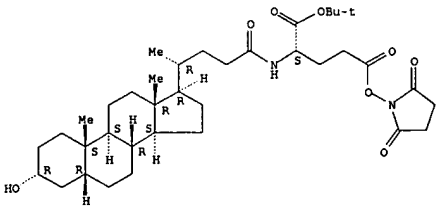
AB GLP-1 derivs. were prepd. and used to prep. pharmaceutical compns. of improved soly. and/or stability. Thus, Arg26,34,Lys36[N.epsilon.-[.gamma.-glutamyl(N.alpha.-hexadecanoyl)]] GLP-1 (7-36)-OH, prepd. via reaction of Arg26,34,Lys36 GLP-1 (7-36)-OH with N.alpha.-hexadecanoylglutamic acid succinimidyl ester, was combined with mannitol and phenol in a pharmaceutical formulation.

IT **240133-29-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of GLP-1 derivs. which form partially structured micellar-like aggregates)

RN 240133-29-3 CAPLUS
CN L-Norvaline, 5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-N-[(3.alpha.,5.beta.)-3-hydroxy-24-oxocholan-24-yl]-5-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 15 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1999:278142 CAPLUS
DOCUMENT NUMBER: 131:110884
TITLE: Modified-Peptide Inhibitors of Amyloid .beta.-Peptide Polymerization
AUTHOR(S): Findeis, Mark A.; Musso, Gary M.; Arico-Muendel, Christopher C.; Benjamin, Howard W.; Hundal, Arvind M.; Lee, Jung-Ja; Chin, Joseph; Kelley, Michael; Wakefield, James; Hayward, Neil J.; Molineaux, Susan M.
CORPORATE SOURCE: PRAECIS Pharm. Inc., Cambridge, MA, 02139-1572, USA
SOURCE: Biochemistry (1999), 38(21), 6791-6800
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cellular toxicity resulting from nucleation-dependent polymn. of amyloid .beta.-peptide (A.beta.) is considered to be a major and possibly the primary component of Alzheimer's disease (AD). Inhibition of A.beta. polymn. has thus been identified as a target for the development of therapeutic agents for the treatment of AD. The intrinsic affinity of A.beta. for itself suggested that A.beta.-specific interactions could be adapted to the development of compds. that would bind to A.beta. and prevent it from polymg. A.beta.-derived peptides of fifteen residues were found to be inhibitory of A.beta. polymn. The activity of these peptides was subsequently enhanced through modification of their amino termini with specific org. reagents. Addnl. series of compds. prepd. to probe structural requirements for activity allowed redn. of the size of the inhibitors and optimization of the A.beta.-derived peptide portion to afford a lead compd., cholyl-Leu-Val-Phe-Phe-Ala-OH (PPI-368), with potent polymn. inhibitory activity but limited biochem. stability. The corresponding all-D-amino acyl analog peptide acid (PPI-433) and amide (PPI-457) retained inhibitory activity and were both stable in monkey cerebrospinal fluid for 24 h.

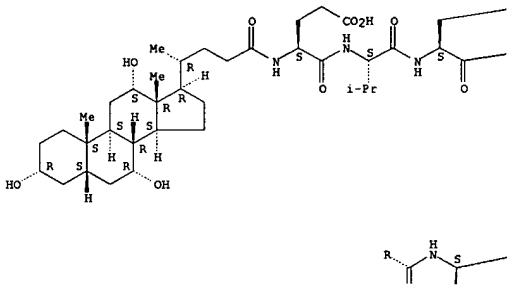
IT **183745-86-0P 183746-15-8P 183746-28-3P 183746-31-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(modified peptide inhibitors of amyloid .beta.-peptide polymn. and stability in monkey CSF)

RN 183745-86-0 CAPLUS
CN Glycine, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-.alpha.-glutamyl-L-valyl-L-histidyl-L-histidyl-L-glutaminyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl-L-phenylalanyl-L-alanyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl-L-valyl- (9CI) (CA INDEX NAME)

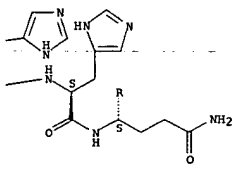
Absolute stereochemistry.

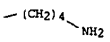
L6 ANSWER 16 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



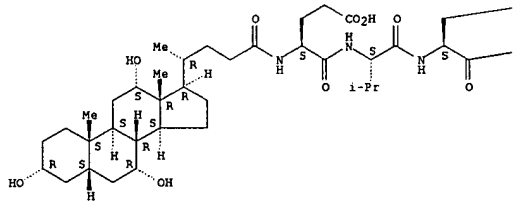


*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 183746-15-8 CAPLUS
CN L-Phenylalanine, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-.alpha.-glutamyl-L-valyl-L-histidyl-L-

L6 ANSWER 16 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
histidyl-L-glutaminyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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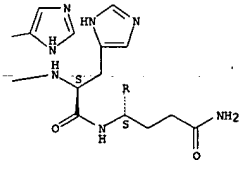
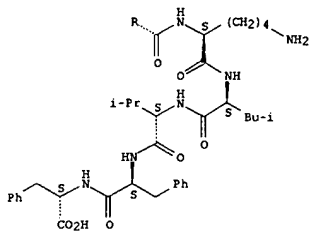


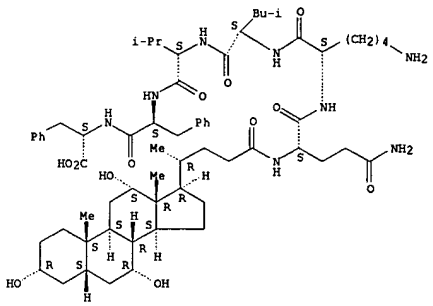
L6 ANSWER 16 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 2-A



RN 183746-28-3 CAPLUS
CN L-Phenylalanine, N2-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-glutaminyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 183746-31-8 CAPLUS
CN L-Phenylalanine, N2-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-glutaminyl-L-lysyl-L-leucyl-L-valyl- (9CI) (CA INDEX NAME)

L6 ANSWER 17 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1999:21679 CAPLUS
DOCUMENT NUMBER: 130:95847
TITLE: Preparation of amyloid .beta. peptides and derivatives that modulate .beta.-amyloid aggregation
INVENTOR(S): Findeis, Mark A.; Benjamin, Howard; Garnick, Marc B.; Gefter, Malcolm L.; Hundal, Arvind; Kasman, Laura; Musso, Gary; Signet, Ethan R.; Wakefield, James; Reed, Michael; Molineaux, Susan; Kubasek, William; Chin, Joseph; Lee, Jung-Ja; Kelley, Michael
PATENT ASSIGNEE(S): Praecis Pharmaceuticals, Inc., USA
SOURCE: U.S., 52 pp., Cont.-in-part of U.S. Ser. No. 404,831.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5854204	A	19981229	US 1996-612785	19960314
US 5817626	A	19981006	US 1995-404831	19950314
US 5854215	A	19981229	US 1995-475579	19950607
AU 759036	B2	20030403	AU 2000-35389	20000519

PRIORITY APPLN. INFO.: US 1995-404831 A2 19950314
US 1995-475579 A2 19950607
US 1995-548998 A2 19951027
AU 1996-52524 A3 19960314

AB Compds. that modulate the aggregation of amyloidogenic proteins or peptides are disclosed. The modulators of the invention can promote amyloid aggregation or, more preferably, can inhibit natural amyloid aggregation. In a preferred embodiment, the compds. modulate the aggregation of natural .beta. amyloid peptides (.beta.-AP). In a preferred embodiment, the .beta. amyloid modulator compds. of the invention are comprised of an A.beta.-aggregation core-domain and a modifying group coupled thereto such that the compd. alters the aggregation or inhibits the neurotoxicity of natural .beta. amyloid peptides when contacted with the peptides. Furthermore, the modulators are capable of altering natural .beta.-AP aggregation when the natural .beta.-APs are in a molar excess amt. relative to the modulators. Pharmaceutical compns. comprising the compds. of the invention, and diagnostic and treatment methods for amyloidogenic diseases using the compds. of the invention, are also disclosed.

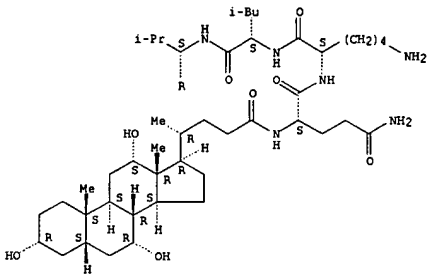
IT **183745-86-0P 183746-15-8P 183746-28-3P 183746-31-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amyloid .beta. peptides and derivs. that modulate .beta.-amyloid aggregation)

RN 183745-86-0 CAPLUS
CN Glycine, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-.alpha.-glutamyl-L-valyl-L-histidyl-L-histidyl-L-glutaminyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl-L-phenylalanyl-L-alanyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl-L-valyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 16 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
Absolute stereochemistry.

PAGE 1-A



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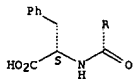
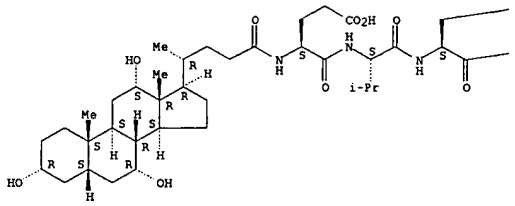
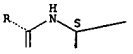


REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 17 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-A





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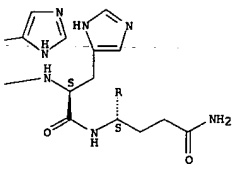

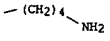

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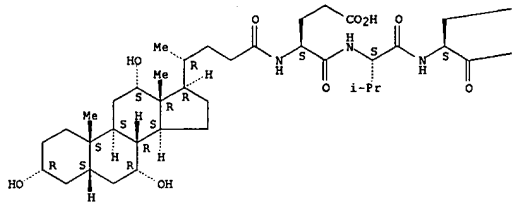
RN 183746-15-8 CAPLUS
CN L-Phenylalanine, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-.alpha.-glutamyl-L-valyl-L-histidyl-L-

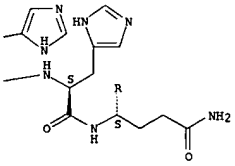
L6 ANSWER 17 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
histidyl-L-glutaminyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

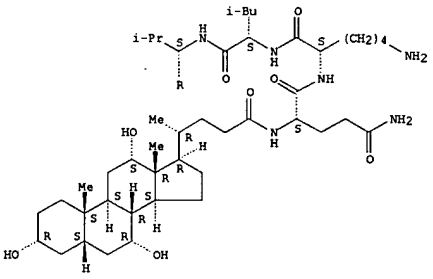


PAGE 1-B



L6 ANSWER 17 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
Absolute stereochemistry.

PAGE 1-A



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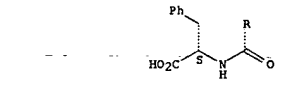
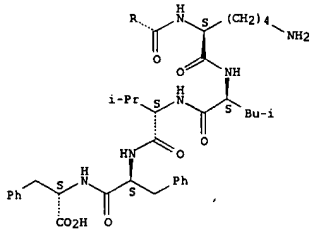


REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

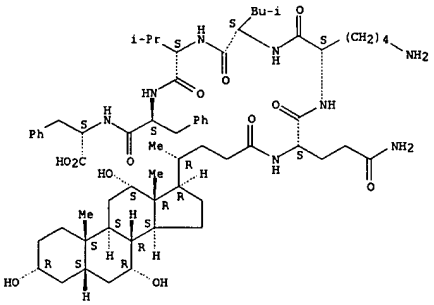
L6 ANSWER 17 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 2-A



RN 183746-28-3 CAPLUS
CN L-Phenylalanine, N2-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-glutaminyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

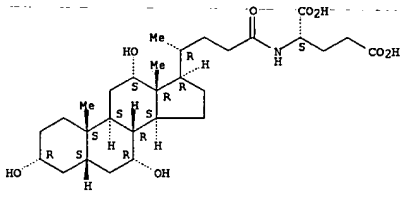
Absolute stereochemistry.



RN 183746-31-8 CAPLUS
CN L-Phenylalanine, N2-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-glutaminyl-L-lysyl-L-leucyl-L-valyl- (9CI) (CA INDEX NAME)

L6 ANSWER 18 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:765933 CAPLUS
DOCUMENT NUMBER: 130:172907
TITLE: In vitro absorption studies of ibuprofen with cholic and deoxycholic acid conjugates
AUTHOR(S): Vishwakarma, K. K.; Kohli, D. V.; Uppadhyay, R. K.
CORPORATE SOURCE: Department of Pharmaceutical Sciences, Dr. H. S. Gour Vishwavidyalaya, Sagar, 470 003, India
SOURCE: Indian Journal of Pharmaceutical Sciences (1998), 60(3), 149-152
CODEN: IJSIDW; ISSN: 0250-474X
PUBLISHER: Indian Pharmaceutical Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cholic acid and deoxycholic acid were conjugated with glutamic acid to prep. N-[3.alpha.,7.alpha.,12.alpha.-trihydroxy-24-oxocholan-24-yl]glutamic acid and N-[3.alpha.,12.alpha.-24-oxocholan-24-yl]glutamic acid. Deoxycholic acid was conjugated with .alpha.-alanine to prep. N-[3.alpha.,12.alpha.-dihydroxy 24-oxocholan-24-yl]-.alpha.-alanine. The sodium salt of cholic acid and deoxycholic acid conjugates were then prepd. and evaluated for surface activity and emulsifying properties. The effect of these compds. on in vitro absorption of ibuprofen was also investigated. All the biosurfactants enhanced the in vitro absorption of ibuprofen.
IT **220362-70-9P 220362-75-4P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(absorption of ibuprofen with cholic and deoxycholic acid conjugates)
RN 220362-70-9 CAPLUS
CN L-Glutamic acid, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-, disodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

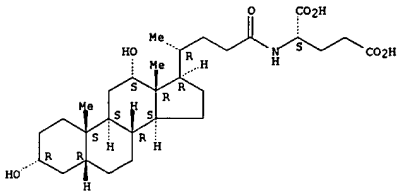


●2 Na

RN 220362-75-4 CAPLUS
CN L-Glutamic acid, N-[(3.alpha.,5.beta.,12.alpha.)-3,12-dihydroxy-24-oxocholan-24-yl]-, disodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

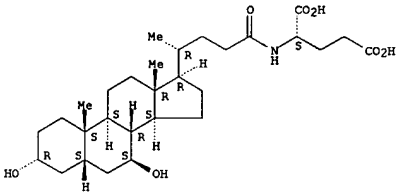
L6 ANSWER 18 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



●2 Na

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 19 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 19 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:400309 CAPLUS
DOCUMENT NUMBER: 129:170489
TITLE: Basic studies on N"-ursodeoxycholyldiethylenetriamine-N,N,N'-triacetic acid for the dissolution of calcified gallstones
AUTHOR(S): Takahashi, Makoto; Konishi, Toshio; Maeda, Yorinobu; Fukuzawa, Masataka; Nishida, Toshihiro; Ohya, Toshihide; Katayama, Kouji; Kakehi, Norihiko; Sakakura, Hiroo; Takagi, Atsushi; Maeda, Minoru; Ohama, Hirobumi
CORPORATE SOURCE: Department of Surgery, Chugoku Rosai Hospital, Hiroshima, 737-01, Japan
SOURCE: Biological & Pharmaceutical Bulletin (1998), 21(6), 551-557
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A novel calcium-chelating agent, N"-ursodeoxycholyldiethylenetriamine-N,N,N'-triacetic acid (UDCA-DTTA), was synthesized to study its ability to dissolve calcified gallstones. The chelating activity of the compd. was demonstrated by dissolving calcium carbonate in vitro at a high dissoln. rate. In the presence of the agent, sliced human gallstone with a compn. of more than 50% calcium bilirubinate was thoroughly dissolved, indicating that calcium bilirubinate was dissolved from the gallstone. The ability to dissolve calcium was comparable to that of EDTA. However, the laminar structure of the sliced gallstone did not disappear in the presence of EDTA, whereas the structure disappeared in the presence of UDCA-DTTA. All these results indicate that UDCA-DTTA is an interesting compd. as a parent substance for developing a prodrug for an oral or i.v. agent to dissolve calcium-contg. gallstones.
IT **99956-35-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(ursodeoxycholyldiethylenetriamine triacetic acid for calcified gallstone dissoln., and prepn. thereof)
RN 99956-35-1 CAPLUS
CN L-Glutamic acid, N-[(3.alpha.,5.beta.,7.beta.)-3,7-dihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

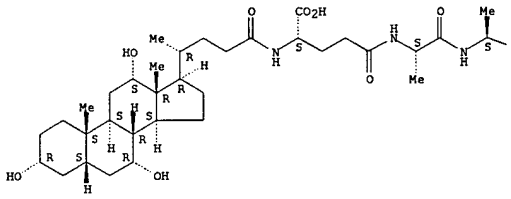
Absolute stereochemistry.

L6 ANSWER 20 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:433596 CAPLUS
DOCUMENT NUMBER: 127:70711
TITLE: Enhanced Transepithelial Transport of Peptides by Conjugation to Cholic Acid
AUTHOR(S): Swaan, Peter W.; Hillgren, Kathleen M.; Szoka, Francis C. Jr.; Oie, Svein
CORPORATE SOURCE: Department of Biopharmaceutical Sciences, University of California at San Francisco, San Francisco, CA, 94143-0446, USA
SOURCE: Bioconjugate Chemistry (1997), 8(4), 520-525
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The potential of the intestinal bile acid transporter to serve as a shuttle for small peptide mols. was investigated. Eleven peptides with a 2-6 amino acid backbone were conjugated to the 24-position of 3.alpha.,7.alpha.,12.alpha.-trihydroxy-5.beta.-cholan-24-oic acid (cholic acid) via an amide bond using an automated peptide synthesizer. In a human intestinal cell line (CaCo-2), cholic acid-peptide conjugates were able to inhibit the transepithelial transport of [3H]taurocholic acid, a natural substrate for the bile acid carrier, at a 100:1 conjugate/substrate ratio. Affinity for the carrier decreased significantly when the conjugate in the 24-position increased from 1 to 2 amino acids. Further increase in the amino acid chain length caused only minor decrease in affinity. A tetrapeptide-bile acid conjugate, [3H]ChEAAA (Ch = cholic acid), was transported by the bile acid transporter, showing markedly higher apical (AP)-to-basolateral (BL) compared to BL-to-AP transport and inhibition by a 100-fold excess taurocholic acid. Another conjugate with 6 amino acids (ChEASASA) was transported by a passive diffusion pathway but still showed higher transport rates than the passive permeability marker mannitol, suggesting the possibility that the cholic acid moiety aids the passive membrane transfer of peptide mols. by increasing its lipophilicity. Metab. of bile acid-peptide conjugates in CaCo-2 cells was 3% over 3 h. In conclusion, these studies show that the coupling of peptides to the 24-position of the sterol nucleus in cholic acid results in a combination of decreased metab. and increased intestinal absorption, either by a carrier-mediated pathway or by accelerated passive diffusion.
IT **191528-84-4 191528-85-5 191528-87-7 191528-88-8 191528-89-9 191528-90-2 191528-91-3 191528-92-4 191528-93-5 191528-94-6**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(enhanced transepithelial transport of peptides by conjugation to cholic acid)
RN 191528-84-4 CAPLUS
CN L-Alaninamide, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-.gamma.-glutamyl-L-alanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 20 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-A



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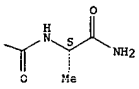
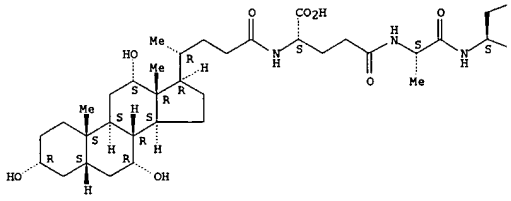


RN 191528-85-5 CAPLUS
CN L-Alaninamide, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-.gamma.-glutamyl-L-alanyl-L-seryl-L-alanyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



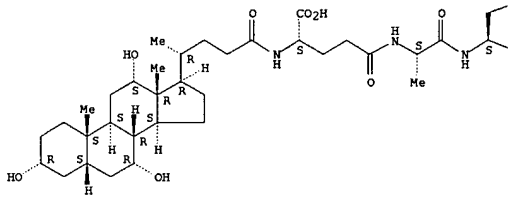
L6 ANSWER 20 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-B

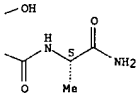
RN 191528-89-9 CAPLUS
CN L-Alaninamide, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-.gamma.-glutamyl-L-alanyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

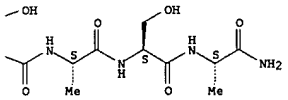


RN 191528-90-2 CAPLUS
CN L-Alaninamide, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-.gamma.-glutamyl-L-alanyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

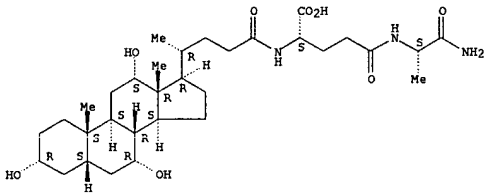
L6 ANSWER 20 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-B



RN 191528-87-7 CAPLUS
CN L-Alaninamide, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-.gamma.-glutamyl- (9CI) (CA INDEX NAME)

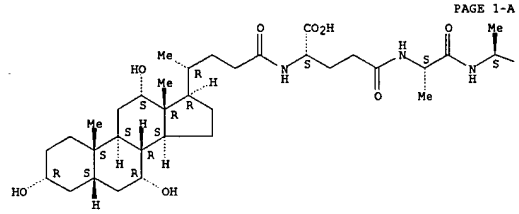
Absolute stereochemistry.



RN 191528-88-8 CAPLUS
CN L-Alaninamide, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-.gamma.-glutamyl-L-alanyl- (9CI) (CA INDEX NAME)

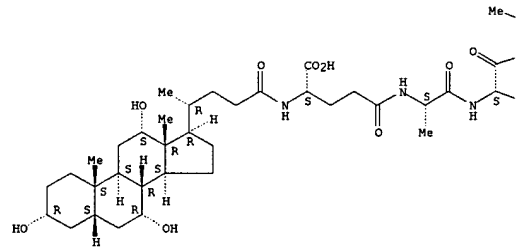
Absolute stereochemistry.

PAGE 1-A

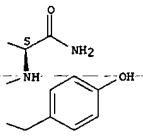


L6 ANSWER 20 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

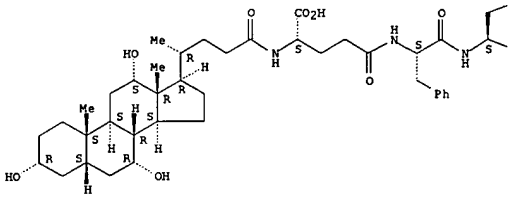


RN 191528-91-3 CAPLUS
CN L-Alaninamide, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-.gamma.-glutamyl-L-phenylalanyl-L-seryl- (9CI) (CA INDEX NAME)

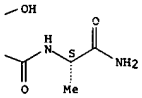
Absolute stereochemistry.

L6 ANSWER 20 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-A



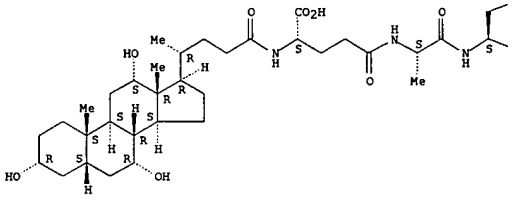
PAGE 1-B



RN 191528-92-4 CAPLUS
CN L-Alaninamide, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-.gamma.-glutamyl-L-alanyl-L-seryl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

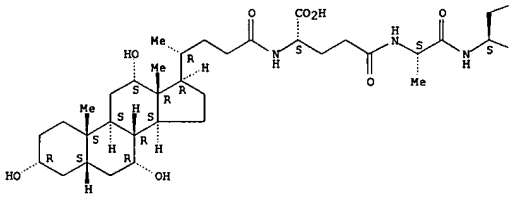
PAGE 1-A



L6 ANSWER 20 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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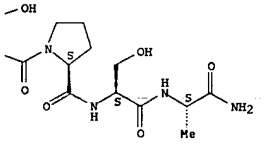
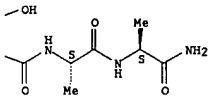


L6 ANSWER 20 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

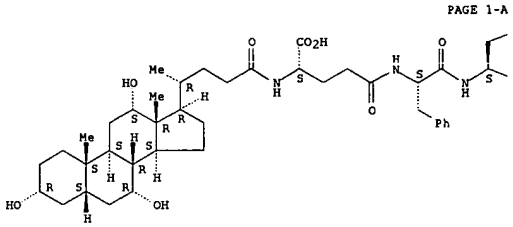
PAGE 1-B



RN 191528-93-5 CAPLUS
CN L-Alaninamide, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-.gamma.-glutamyl-L-phenylalanyl-L-seryl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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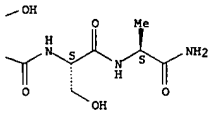


RN 191528-94-6 CAPLUS
CN L-Alaninamide, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-.gamma.-glutamyl-L-alanyl-L-seryl-L-prolyl-L-seryl-

L6 ANSWER 21 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1997:218959 CAPLUS
DOCUMENT NUMBER: 126:308684
TITLE: Use of the intestinal bile acid transporter for the uptake of cholic acid conjugates with HIV-1 protease inhibitory activity
AUTHOR(S): Kagedahle, Matts; Swaan, Peter W.; Redemann, Carl T.; Tang, Mary; Craik, Charles S.; Szoka, Francis C., Jr.; Oie, Svein
CORPORATE SOURCE: Dep. Pharmacy Pharmaceutical Chem., Univ. California, San Francisco, CA, 94143-0446, USA
SOURCE: Pharmaceutical Research (1997), 14(2), 176-180
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Plenum
DOCUMENT TYPE: Journal
LANGUAGE: English

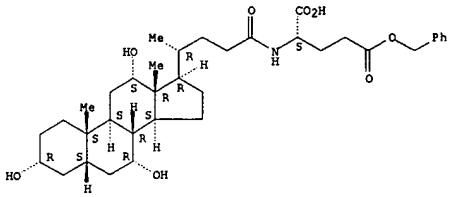
AB The purpose of this study was to investigate the ability of the human intestinal bile acid transporter to transport cholic acid conjugates with potential HIV-1 protease inhibitory activity. Cholic acid was conjugated at the 24 position of the sterol nucleus with various amino acids and amino acid analogs. The CaCo-2 cell line was used as a model to investigate the interaction of these bile acid conjugates with the human intestinal bile acid transporter. Interaction between the carrier and the conjugates was quantified by inhibition of taurocholic acid transport and confirmed by transport of radiolabeled conjugates in this cell line. The highest interaction with the transporter, as quantified by inhibition of taurocholic acid transport, occurred when a single neg. charge was present around the 24 to 29 region of the sterol nucleus. A second neg. charge or a pos. charge significantly reduced the interaction. Transport of radiolabeled cholyl-L-Lys-.epsilon.-tBOC ester and cholyl-D-Asp-.beta.-benzyl ester was inhibited by taurocholic acid. Of all tested compds., only cholyl-D-Asp-.beta.-benzyl ester showed modest HIV-1 protease inhibitory activity with an IC50 of 125 .mu.M. Cholic acid-amino acid conjugates with appropriate stereochem. are recognized and transported by the human bile acid transporter and show modest HIV-1 protease inhibitory activity. Transport of these conjugates by the bile acid carrier is influenced by charge and hydrophobicity around the 24 position of the sterol nucleus.

IT **189261-15-2P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

RN 189261-15-2 CAPLUS
CN L-Glutamic acid, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-, 5-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 21 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L6 ANSWER 22 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1996:748345 CAPLUS
DOCUMENT NUMBER: 126:19332
TITLE: Preparation of peptides as modulators of amyloid aggregation
INVENTOR(S): Findeis, Mark A.; Benjamin, Howard; Garnick, Marc B.; Gefter, Malcolm L.; Hundal, Arvind; Kasman, Laura; Musso, Gary; Signer, Ethan R.; Wakefield, James; et al.
PATENT ASSIGNEE(S): Pharmaceutical Peptides Incorporated, USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9628471	A1	19960919	WO 1996-US3492	19960314
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5817626	A	19981006	US 1995-404831	19950314
US 5854215	A	19981229	US 1995-475579	19950607
AU 9652524	A1	19961002	AU 1996-52524	19960314
EP 815134	A1	19980107	EP 1996-908805	19960314
EP 815134	B1	20020605		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11514333	T2	19991207	JP 1996-527816	19960314
AT 218583	E	20020615	AT 1996-908805	19960314
AU 759036	B2	20030403	AU 2000-35389	20000519

PRIORITY APPLN. INFO.:
US 1995-404831 A 19950314
US 1995-475579 A 19950607
US 1995-548998 A 19951027
AU 1996-52524 A3 19960314
WO 1996-US3492 W 19960314

AB Compds. that modulate the aggregation of amyloidogenic proteins or peptides are disclosed. The modulators of the invention can promote amyloid aggregation or, more preferably, can inhibit natural amyloid aggregation. In a preferred embodiment, the compds. modulate the aggregation of natural .beta. amyloid peptides (.beta.-AP). In a preferred embodiment, the .beta. amyloid modulator compds. of the invention are comprised of an A.beta. aggregation core domain and a modifying group coupled thereto such that the compd. alters the aggregation or inhibits the neurotoxicity of natural .beta. amyloid peptides when contacted with the peptides. Furthermore, the modulators are capable of altering natural .beta.-AP aggregation when the natural .beta.-APs are in a molar excess amt. relative to the modulators. Pharmaceutical compns. comprising the compds. of the invention, and diagnostic and treatment methods for amyloidogenic diseases using the compds. of the invention, are also disclosed. These peptide compds. are bound to natural .beta.-amyloid peptides to facilitate diagnosis of a .beta.-amyloidogenic disease, in particular Alzheimer's disease, and are useful for treating a disorder assocd. with amyloidosis including, e.g. familial amyloid polyneuropathy or cardiomyopathy, isolated cardiac amyloid, systemic senile amyloidosis, scrapie, bovine spongiform

L6 ANSWER 22 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

encephalopathy, and Creutzfeldt-Jakob disease. Thus, N-biotinyl-DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVV-OH (N-biotinyl-.beta.-AP1-40), prepd. by the solid phase synthesis using a N.alpha.-Fmoc-based protection strategy and Fmoc-Val-Wang resin, at 1% markedly inhibited aggregation of the natural .beta.-amyloid peptide (.beta.-AP1-40).

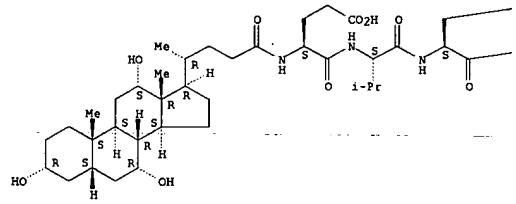
IT **183745-86-0P 183746-15-8P 183746-28-3P**
183746-31-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptides as modulators of amyloid aggregation for treating amyloidosis-assocd. disorders)

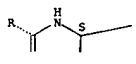
RN 183745-86-0 CAPLUS

CN Glycine, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-.alpha.-glutamyl-L-valyl-L-histidyl-L-histidyl-L-glutaminyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl-L-phenylalanyl-L-alanyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl-L-valyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

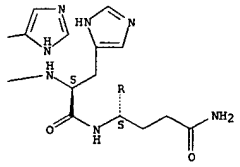
PAGE 1-A

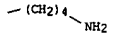




L6 ANSWER 22 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-B





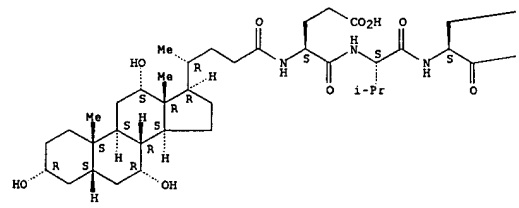
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 183746-15-8 CAPLUS

CN L-Phenylalanine, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-.alpha.-glutamyl-L-valyl-L-histidyl-L-histidyl-L-glutaminyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

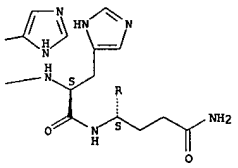
Absolute stereochemistry.

PAGE 1-A

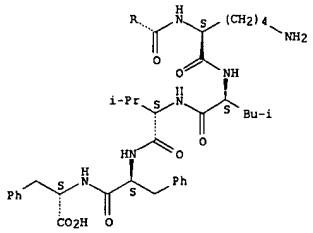


L6 ANSWER 22 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-B



PAGE 2-A

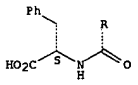


RN 183746-28-3 CAPLUS
CN L-Phenylalanine, N2-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-glutaminyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

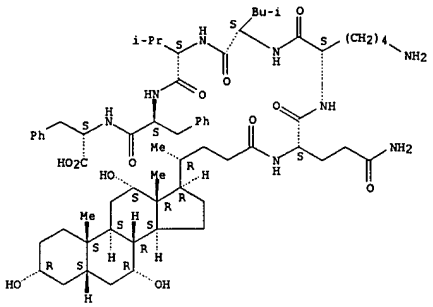
Absolute stereochemistry.

L6 ANSWER 22 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 2-A



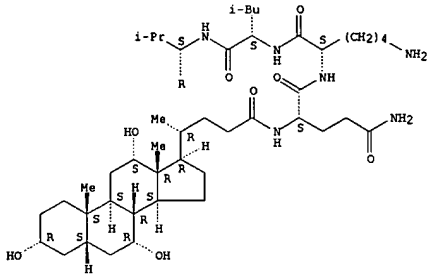
L6 ANSWER 22 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 183746-31-8 CAPLUS
CN L-Phenylalanine, N2-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-glutaminyl-L-lysyl-L-leucyl-L-valyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



L6 ANSWER 23 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1995:721131 CAPLUS
DOCUMENT NUMBER: 123:322102
TITLE: Acylated derivatives of human insulin with improved solubility and stability for treatment of diabetes
INVENTOR(S): Havelund, Svend; Halstroem, John Broberg; Jonassen, Ib; Andersen, Asser Sloth; Markussen, Jan
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9507931	A1	19950323	WO 1994-DK347	19940916
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9407187	A	19950317	ZA 1994-7187	19940916
CA 2171424	AA	19950323	CA 1994-2171424	19940916
CA 2171424	C	20020604		
AU 9476520	A1	19950403	AU 1994-76520	19940916
AU 682061	B2	19970918		
CN 1133598	A	19961016	CN 1994-193852	19940916
CN 1056618	B	20000920		
BR 9407508	A	19970107	BR 1994-7508	19940916
HU 75991	A2	19970528	HU 1996-676	19940916
HU 217684	B	20000328		
EP 792290	A1	19970903	EP 1994-926816	19940916
EP 792290	B1	20010829		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
RO 112873	B1	19980130	RO 1996-583	19940916
JP 3014764	B2	20000228	JP 1995-508923	19940916
JP 09502867	T2	19970325		
JP 2000060556	A2	20000229	JP 1999-221632	19940916
PL 178466	B1	20000531	PL 1994-313444	19940916
IL 110977	A1	20000629	IL 1994-110977	19940916
CZ 287945	B6	20010314	CZ 1996-789	19940916
RU 2164520	C2	20010327	RU 1996-108249	19940916
EP 1132404	A2	20010912	EP 2001-112992	19940916
EP 1132404	A3	20020327		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT				
AT 204882	E	20010915	AT 1994-926816	19940916
ES 2163451	T3	20020201	ES 1994-926816	19940916
SK 282495	B6	20020205	SK 1996-324	19940916
JP 2002308899	A2	20021023	JP 2001-385921	19940916
FI 9601220	A	19960514	FI 1996-1220	19960315
NO 9601070	A	19960515	NO 1996-1070	19960315
AU 9748461	A1	19980219	AU 1997-48461	19971218
AU 745983	B2	20020411	AU 2000-51960	20000811

PRIORITY APPLN. INFO.:
DK 1993-1044 A 19930917
US 1994-190829 A 19940202
EP 1994-926816 A3 19940916
JP 1995-508923 A3 19940916
JP 1999-221632 A3 19940916

L6 ANSWER 23 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
WO 1994-DK347 W 19940916

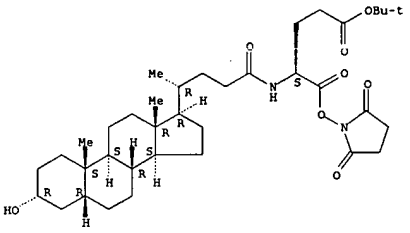
AB Novel human insulin derivs. with improved soly. and a protracted profile of action are described for use in the treatment of diabetes. These analogs have amino acid substitutions at amino acids A21 and B3 (any amino acid except Lys, Arg, or Cys); PheB1 may be deleted and B30 is substituted by a C10-24 lipophilic amino acid or any naturally occurring amino acid except Lys, Arg, or Cys; if B30 is a lipophilic amino acid, then the .epsilon.-NH2 group of LysB29 is acylated with a C.ltoreq.5 carboxylic acid. They may be used in the treatment of diabetes in several pharmaceutical compns. presented. Chem. prepn. of some of these analogs and the manuf. of the amino acid-substituted A and B chains by expression of the cloned cDNAs is demonstrated.

IT **168986-19-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylated derivs. of human insulin with improved soly. and stability for treatment of diabetes)

RN 168986-19-4 CAPLUS

CN Pentanoic acid, 5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-[[(3.alpha.,5.beta.)-3-hydroxy-24-oxocholan-24-yl]amino]-5-oxo-, 1,1-dimethylethyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 24 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1994:631137 CAPLUS
DOCUMENT NUMBER: 121:231137
TITLE: Electron impact ionization mass spectra of lithocholyl amides: evidences for a C(20) to C(23) rearrangement involving the loss of a C4H9 fragment
AUTHOR(S): Nair, Padmanabhan P.; Flanagan, Vincent P.; Oliver, James E.
CORPORATE SOURCE: Beltsville Human Nutrition Res. Center, Agricultural Research Service, Beltsville, MD, 20705, USA
SOURCE: Organic Mass Spectrometry (1994), 29(7), 335-41
CODEN: ORMSBG; ISSN: 0030-493X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Amides of lithocholic acid (3.alpha.-hydroxy-5.beta.-cholan-24-oic acid) with 6-aminocaproic acid and 4-aminobutyric acid were prepd. and examd. by electron impact ionization mass spectrometry. Both these compds. gave an unusual [M - 57]+ fragment. Since the product-ion anal. of [M - 57]+ revealed the presence of fragments corresponding to the intact steroid nucleus in addn. to that of the original amino acid (6-aminocaproic acid or 4-aminobutyric acid), we concluded that the integrity of the steroid amide had been retained in this fragment. The absence of this fragment from the prodn.-ion spectrum of [M - CH3]+ rules out the sequential loss from the mol. ion of 15 + 42 u as the origin of this signal. Mass spectrometry of the 24-13C-labeled lithocholylcaproylamide showed the retention of the label in the [M - 57]+ fragment. In contrast, the corresponding compd. labeled with deuterium at C(23) showed a significant loss of the label during the formation of this product ion at [M - 58]+. In addn., through a combination of derivatization and tandem mass spectrometry, it was demonstrated that this loss of 57 u represented a rearrangement with the expulsion of a C4H9 radical from the side-chain spanning C(20) to C(23) resulting a truncated steroid-amide fragment. This fragmentation pattern has not been obsd. in bile acid conjugates with .alpha.-amino acids.

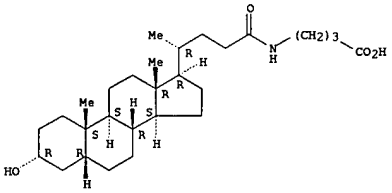
IT **158300-77-7**
RL: PRP (Properties)
(electron impact ionization mass spectrum of)

RN 158300-77-7 CAPLUS

CN Butanoic acid, 4-[[(3.alpha.,5.beta.)-3-hydroxy-24-oxocholan-24-yl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 24 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L6 ANSWER 25 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1991:182667 CAPLUS
DOCUMENT NUMBER: 114:182667
TITLE: Specificity of the hepatocyte sodium-dependent taurocholate transporter: influence of side chain length and charge
AUTHOR(S): Hardison, William G. M.; Heasley, Victor L.; Shellhamer, Dale F.
CORPORATE SOURCE: Veterans Adm. Med. Cent., San Diego, CA, 92161, USA
SOURCE: Hepatology (Philadelphia, PA, United States) (1991), 13(1), 68-72
CODEN: HPTLD9; ISSN: 0270-9139
DOCUMENT TYPE: Journal
LANGUAGE: English

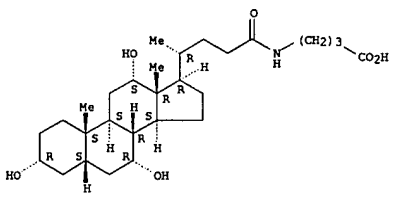
AB Trihydroxy bile acids with differing nonsterol chain length and charge were synthesized to define the effect of these parameters on the ability to inhibit competitively the Na+-dependent uptake of [14C]taurocholate into isolated rat hepatocytes. Compds. with long side chains (.gtoreq.0.8 nm) beyond C-17 of the sterol nucleus and carrying a neg. charge or no charge were potent inhibitors. Introduction of a pos. charge into the side chain weakened inhibition. When the length of the chain beyond C-17 fell below .apprx.0.7 nm, charge still influenced inhibitory potency, but the effect was reversed and pos. charged chains yielded slightly greater inhibition than neg.-charged chains. A pos.-charged cell surface domain extending outward from a point .apprx.0.7 nm from the sterol nucleus receptor region may be postulated. Up to .apprx.0.7 nm from the sterol nucleus receptor region a neg. cell surface charge may be postulated to account for the weaker inhibitory potency of compds. with short neg. charged chains. Nonetheless, a short chain, regardless of charge, weakened inhibition, suggesting that a long neg.-charged side chain is necessary to orient the sterol moiety for optimal receptor fit. These data confirm that the Na+-dependent taurocholate transport site is sensitive to alterations of side chain charge and length and emphasize the importance of structure when designing bile acid analogs to probe taurocholate transport mechanisms.

IT **89311-02-4**
RL: PRP (Properties)
(sodium-dependent taurocholate transport inhibition by and uptake kinetics of, in hepatocytes, side chain length and charge in relation to)

RN 89311-02-4 CAPLUS

CN Butanoic acid, 4-[[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

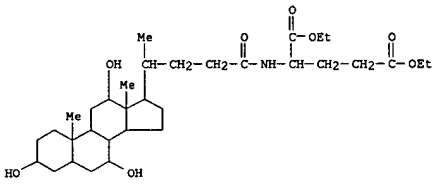


L6 ANSWER 25 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

L6 ANSWER 26 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:570606 CAPLUS
DOCUMENT NUMBER: 111:170606
TITLE: Chromatographic fractionation and quantitation of bile acids
INVENTOR(S): Iwakawa, Masaharu; Horii, Norihito
PATENT ASSIGNEE(S): Sekisui Chemical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63152996	A2	19880625	JP 1986-299321	19861216
JP 07016439	B4	19950301		

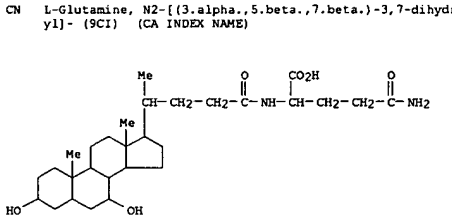
PRIORITY APPLN. INFO.: JP 1986-299321 19861216
AB A method for sepn. and quantitation of bile acids involves: (a) introducing a sample contg. bile acids, with addn. of a (partial) hydrolyzate of the condensation product of a free bile acid and an acidic amino acid ester as internal std., on a separatory column, (b) introducing the eluate mixed with a test reagent on an immobilized-enzyme column, and (c) measuring the reaction product in the 2nd eluate. A serum sample with added internal std. was analyzed by an app. contg. an Enzymepack-HSD column with a fluorometric detector and a reagent contg. KH2PO4, di-Na EDTA, .beta.-NAD, 2-mercaptoethanol, and deionized water.
IT **91021-94-2D**, hydrolyzates
RL: ANST (Analytical study)
(as internal std., for bile acid enzymic-chromatog. detn.)
RN 91021-94-2 CAPLUS
CN L-Glutamic acid, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-, diethyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 27 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:95638 CAPLUS
DOCUMENT NUMBER: 110:95638
TITLE: Ursodeoxycholic acid derivatives and their salts, useful for therapy of biliary conditions, and a process for their preparation
INVENTOR(S): Reiner, Alberto
PATENT ASSIGNEE(S): Jago Research A.-G., Switz.
SOURCE: Eur. Pat. Appl., 7 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 272462	A1	19880629	EP 1987-117184	19871121
EP 272462	B1	19920610		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CH 674369	A	19900531	CH 1986-4729	19861126
US 4865765	A	19890912	US 1987-121257	19871116
AT 77094	E	19920615	AT 1987-117184	19871121
ES 2042530	T3	19931216	ES 1987-117184	19871121

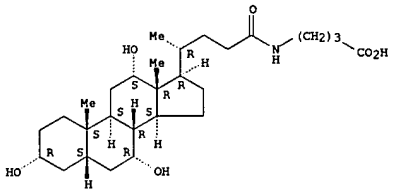
PRIORITY APPLN. INFO.: CH 1986-4729 19861126
EP 1987-117184 19871121
OTHER SOURCE(S): MARPAT 110:95638
AB Title derivs. I [R = CH2SO3H, CO2H; R1 = H, (CH2)2CONH2, CH2CONH2, (CH2)2SMe, CH2SCH2CO2H] and their salts are prepd. for use as biliary therapeutics (no data). A suspension of ursodeoxycholic acid (II) in dioxane at 0-10.degree. was treated with ClCO2Et, and then with a soln. of Et3N in dioxane. The mixt. was warmed to room temp., treated with an aq. methionine amine salt (e.g., with Et3N), and cooled. The temp. was allowed to rise to 27-29.degree. over 5 h with evolution of CO2 (g). Extn. and pptn. with acid gave I [R = CO2H, R1 = (CH2)2SMe] contg. <0.3% free II.
IT **119059-83-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as biliary therapeutic)
RN 119059-83-5 CAPLUS
CN L-Glutamine, N2-[(3.alpha.,5.beta.,7.beta.)-3,7-dihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)



L6 ANSWER 28 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1986:621495 CAPLUS
DOCUMENT NUMBER: 105:221495
TITLE: Influence of the amino acid moiety on deconjugation of bile acid amidates by cholylglycine hydrolase or human fecal cultures
AUTHOR(S): Huijghebaert, Suzanne M.; Hofmann, Alan F.
CORPORATE SOURCE: Dep. Med., Univ. California, San Diego, CA, 92103, USA
SOURCE: Journal of Lipid Research (1986), 27(7), 742-52
CODEN: JLPRAW; ISSN: 0022-2275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The influence of the chem. structure of the amino acid (or amino acid analog) moiety of a no. of synthetic cholyl amidates on deconjugation by cholylglycine hydrolase from Clostridium perfringens was studied in vitro at pH 5.4. Conjugates with alkyl homologs of glycine were hydrolyzed more slowly as the no. of methylene units increased (cholylglycine > cholyl-.beta.-alanine > cholyl-.gamma.-aminobutyrate). In contrast, for conjugates with the alkyl homologs of taurine, cholylaminopropane sulfonate was hydrolyzed slightly faster than cholyltaurine, whereas cholylaminomethane sulfonate was hydrolyzed much more slowly. When glycine was replaced by other neutral .alpha.-amino acids, rates of hydrolysis decreased with increasing steric hindrance near the amide bond (cholyl-L-.alpha.-alanine >> cholyl-L-leucine >> cholyl-L-valine > cholyl-L-tyrosine >>> cholyl-D-valine). Conjugation with acidic or basic amino acids also greatly reduced the rates of hydrolysis, as cholyl-L-aspartate, cholyl-L-cysteate, cholyl-L-lysine, and cholyl-L-histidine were all hydrolyzed at a rate <0.1-fold that of cholylglycine. Me esterification of the carboxylic group of the amino acid moiety reduced the hydrolysis, but such substrates (cholylglycine Me ester and cholyl-.beta.-alanine Me ester) were completely hydrolyzed after overnight incubation with excess enzyme. In contrast, cholyl-cholamine was not hydrolyzed at all, suggesting that a neg. charge at the end of the side chain is required for optimal hydrolysis. Despite the lack of specificity for the amino acid moiety, a bile salt moiety was required, as the cholylglycine hydrolase did not display general carboxypeptidase activity for other nonbile acid substrates contg. a terminal amide bond; hippuryl-L-phenylalanine, hippuryl-L-arginine, oleyltaurine, and oleylglycine were not hydrolyzed. Fecal bacterial cultures from healthy volunteers also hydrolyzed cholyl-L-valine and cholyl-D-valine more slowly than cholylglycine, suggesting that cholylglycine hydrolase from C. perfringens has a substrate specificity similar to that of the deconjugating enzymes of the fecal flora. Thus, modification of the position of the amide bond, introduction of steric hindrance near the amide bond, or loss of a neg. charge on the terminal group of the amino acid moiety of the bile acid conjugate greatly reduces the rate of bacterial deconjugation in vitro when compared to that of the naturally occurring glycine and taurine conjugates.
IT **89311-02-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrolysis of, by cholylglycine hydrolase of Clostridium perfringens, other bile acid amidates comparison with)
RN 89311-02-4 CAPLUS
CN Butanoic acid, 4-[[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 28 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L6 ANSWER 29 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

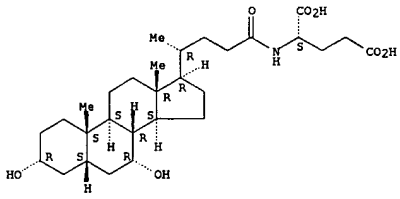
ACCESSION NUMBER: 1986:588698 CAPLUS
DOCUMENT NUMBER: 105:188698
TITLE: Effect of bile acid side chain on dissolution of calcium carbonate
AUTHOR(S): Yoneda, Masashi
CORPORATE SOURCE: Sch. Med., Hirosaki Univ., Hirosaki, Japan
SOURCE: Nippon Shokakibyo Gakkai Zasshi (1986), 83(5), 1063
CODEN: NIPAA4; ISSN: 0369-4259
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB The soly. of insol. Ca salts, esp. CaCO3 in artificial bile solns. contg. phospholipids, cholesterol, and various bile acids was studied. The soly. of 100 mg CaCO3 after incubation at 37.degree. for 3 h in 1 mL artificial bile soln. (50 mM, pH 7.5 Tris buffer contg. 25 mol% phospholipids and 5 mol% cholesterol) contg. 70 mol% glycocholate, glycochenodeoxycholate, taurocholate, taurochenodeoxycholate, aspartylchenodeoxycholate (AspCDCA), and glutamylchenodeoxycholate (GluCDCA) was 3.58, 0.68, 6.36, 6.15, 10.84, and 11.10 mg/dL, resp. The study of CaCO3 appeared to be greater in bile contg. GluCDCA and AspCPCA than in bile contg. the other tested bile acids. Apparently, the soly. of CaCO3 in a bile soln. may be influenced by the bile acid side chain present in the bile soln.

IT **95051-20-0**
RL: BIOL (Biological study)
(of bile, calcium carbonate soly. in relation to)

RN 95051-20-0 CAPLUS
CN L-Glutamic acid, N-[(3.alpha.,5.beta.,7.alpha.)-3,7-dihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 30 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1986:183781 CAPLUS
DOCUMENT NUMBER: 104:183781
TITLE: Pancreatic carboxypeptidase hydrolysis of bile acid-amino acid conjugates: selective resistance of glycine and taurine amidates
AUTHOR(S): Huijghebaert, S. M.; Hofmann, A. F.
CORPORATE SOURCE: Sch. Med., Univ. California, San Diego, La Jolla, CA, 92093, USA
SOURCE: Gastroenterology (1986), 90(2), 306-15
CODEN: GASTAB; ISSN: 0016-5085
DOCUMENT TYPE: Journal
LANGUAGE: English

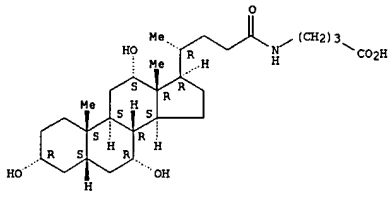
AB To find a possible explanation for the selective hepatic conjugation of bile acids with glycine or taurine, the N-acyl amidates of cholic acid and a no. of amino acids and amino acid analogs were synthesized, and their susceptibility to hydrolysis by pancreatic juice, gastric juice, serum, or small intestinal mucosal enzymes was measured. Deconjugation by pure carboxypeptidase A and B was also examd., and hydrolysis by these tissue fluids and enzymes was compared with that mediated by a bacterial cholylglycine hydrolase. Human pancreatic juice efficiently hydrolyzed cholyl conjugates of all neutral L-amino acids (cholyl-L-alanine, cholyl-L-valine, cholyl-L-leucine, and cholyl-L-tyrosine), except cholylglycine. The net hourly rate of hydrolysis (in micromoles/mg protein/h) increased when the terminal residue was arom. or branched aliph. and appeared to be specific for L-.alpha.-amino acids as cholyl-L-alanine and cholyl-D-valine were not cleaved. From cholyl glycylglycine, only the terminal glycine was efficiently removed. Cholyltaurine and cholyl conjugates with the Me and Pr analogs of taurine were resistant to hydrolysis. Two basic amino acid conjugates (cholyl-L-lysine and cholyl-L-arginine) were cleaved, whereas conjugates of acidic amino acids (cholyl-aspartate and cholyl-cysteate) were not cleaved. Studies with pure enzymes showed that bovine carboxypeptidase A hydrolyzed the cholyl conjugates of the neutral L-.alpha.-amino acids with similar specificity as obsd. for the human pancreatic juice, whereas bovine carboxypeptidase B cleaved the basic amino acid conjugates. Cholyl-L-lysine and cholyl-L-arginine were also cleaved by serum and plasma, which are known to possess carboxypeptidase activity. Cholyl conjugates were not cleaved by gastric juice, trypsin, or homogenates of rat small intestinal mucosa. In contrast, all cholyl conjugates were cleaved by a bacterial cholylglycine hydrolase. Thus, glycine and taurine amidates of cholic acid differ from a no. of other conjugates with neutral and basic amino acids in being resistant to hydrolysis by pancreatic and plasma carboxypeptidases. These data, together with other data indicating that bile acid conjugation greatly decreases passive intestinal absorption, indicate that a physiol. function of bile acid conjugation with glycine or taurine is to form surfactants that remain indigestible and rather nonabsorbable during digestion in the proximal small intestine.

IT **89311-02-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cholylglycine hydrolase hydrolysis of)

RN 89311-02-4 CAPLUS
CN Butanoic acid, 4-[[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 30 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L6 ANSWER 31 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1986:51022 CAPLUS
DOCUMENT NUMBER: 104:51022
TITLE: Chenodeoxycholic acid and ursodeoxycholic acid derivatives
INVENTOR(S): Ito, Masaharu; Yamatsu, Isao; Nezu, Masao; Tateyama, Tadashi; Yoshino, Hiroshi; Kajiwara, Shoji
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 60161996	A2	19850823	JP 1984-15244	19840201

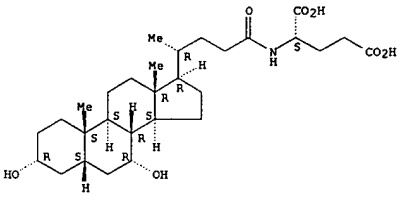
PRIORITY APPLN. INFO.: JP 1984-15244 19840201

AB Title compds. I [R = N(CH2CO2H)2, NHCHR1CO2H, CH(OH)CH2CO2H, CH2OH, CH(OH)Me; R1 = (CH2)nCO2H; n = 1, 2] and pharmacol. permissible salts of I, useful as gallstone dissolving agents, were prepd. by treating I (R = OH) (II) and their acid derivs. with RH (III). Thus, treating chenodeoxycholic acid with NH(CH2CO2H)2 in the presence of NEt3 under stirring at room temp. for 1 h gave 44% N-chenodeoxycholyl-N-carboxymethylglycine (IV). A mixt. of II, .alpha.-lecithin, and cholesterol (pH 7.4) dissolved CaCO3 by 38.2 mg/dL.

IT 95051-20-0P 99956-35-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as gallstone dissolving agents)

RN 95051-20-0 CAPLUS
CN L-Glutamic acid, N-[(3.alpha.,5.beta.,7.alpha.)-3,7-dihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

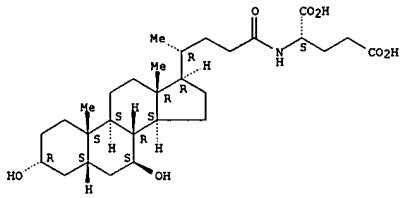
Absolute stereochemistry.



RN 99956-35-1 CAPLUS
CN L-Glutamic acid, N-[(3.alpha.,5.beta.,7.beta.)-3,7-dihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 31 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L6 ANSWER 32 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1985:109384 CAPLUS
DOCUMENT NUMBER: 102:109384
TITLE: Quantitative determination of bile acids
PATENT ASSIGNEE(S): Sekisui Chemical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 59197858	A2	19841109	JP 1983-73308	19830425
JP 01008305	B4	19890213		

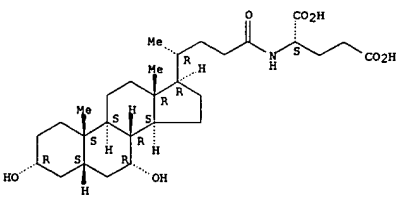
PRIORITY APPLN. INFO.: JP 1983-73308 19830425

AB For the detn. of bile acids in a biol. sample by liq. chromatog., reaction with an immobilized enzyme in a column, and measurement of the products, acidic amino acid conjugates with deoxycholic acid or chenodeoxycholic acid are used as internal stds. Deoxycholic acid-glutamate conjugate was prepd. by reaction of deoxycholic acid with L-glutamic acid di-Et ester HCl. Then 1 mL blood serum with added deoxycholic acid-glutamate conjugate was sepd. on a column packed with octyl group-contg. silica gel to give fractions which were passed through a column with immobilized 3.alpha.-hydroxy steroid dehydrogenase and treated with a reagent contg. NAD+, phosphate buffer (10 mM), EDTA, and 2-mercaptoethanol. The products were measured by fluorometry at 450 nm with excitation at 350 nm. The method was used to det. bile acids in blood serum from patients with acute hepatitis.

IT 95051-20-0P 95051-21-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as internal std. for bile acids detn.)

RN 95051-20-0 CAPLUS
CN L-Glutamic acid, N-[(3.alpha.,5.beta.,7.alpha.)-3,7-dihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

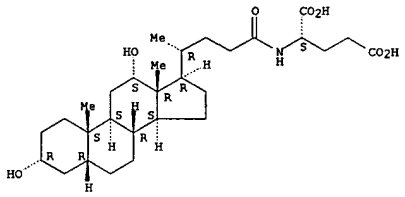
Absolute stereochemistry.



RN 95051-21-1 CAPLUS
CN L-Glutamic acid, N-[(3.alpha.,5.beta.,12.alpha.)-3,12-dihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 32 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L6 ANSWER 33 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1984:420229 CAPLUS
DOCUMENT NUMBER: 101:20229
TITLE: Quantitative determination of bile acids
PATENT ASSIGNEE(S): Sekisui Chemical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 59051349	A2	19840324	JP 1982-162800	19820917
JP 02033360	B4	19900726		

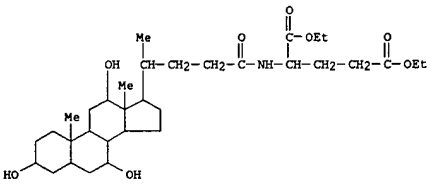
PRIORITY APPLN. INFO.: JP 1982-162800 19820917

AB During the sepn. and quant. detn. of bile acids in a biol. sample by liq. chromatog. and chromatog. on a column contg. immobilized enzymes, amino acid conjugates of cholic acid or ursodeoxycholic acid are added as internal stds. Thus, L-glutamic acid di-Et ester was treated with cholic acid to form a conjugate. The method was used in blood anal. A flow chart of a device for the anal. is presented.

IT **91021-94-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as internal std. for bile acids detn. by liq. chromatog.)

RN 91021-94-2 CAPLUS

CN L-Glutamic acid, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-, diethyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 34 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1984:139568 CAPLUS
DOCUMENT NUMBER: 100:139568
TITLE: Synthesis and spectroscopic analysis of modified bile salts
AUTHOR(S): Ballatore, Annie M.; Beckner, Carl F.; Caprioli, Richard M.; Hoffman, Neville E.; Liehr, Joachim G.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77025, USA
SOURCE: Steroids (1983), 41(2), 197-206
CODEN: STEDAM; ISSN: 0039-128X
DOCUMENT TYPE: Journal
LANGUAGE: English

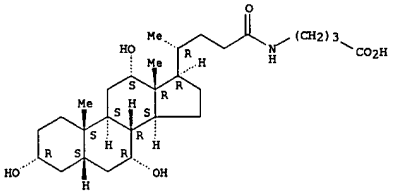
AB The N-cholyl derivs. of leucine, alanine, D-alanine, .beta.-alanine, proline, and .gamma.-aminobutyric acid were prepd. by condensing cholic acid with the appropriate amino acid by ClCO2Et. Structure anal. of the above products were carried out by electron-impact mass spectrometry on the Me ester/acetate derivs., whereas the purity and mol. wt. of the products were detd. by fast-atom mass spectrometry on the underivatized bile salts.

IT **89311-02-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and fast-atom bombardment mass spectrum of)

RN 89311-02-4 CAPLUS

CN Butanoic acid, 4-[[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 35 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1981:117377 CAPLUS
DOCUMENT NUMBER: 94:117377
TITLE: Conjugates from ligand analog and irreversible enzyme inhibitor and their use in determining ligands
INVENTOR(S): Voss, Houston Frederick; Plattner, Jacob; Herrin, Thomas Raymond
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: Ger. Offen., 68 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3003959	A1	19800814	DE 1980-3003959	19800204
DE 3003959	C2	19821223		
US 4273866	A	19810616	US 1979-9007	19790205
CA 1137077	A1	19821207	CA 1980-343676	19800115
AU 8054763	A1	19800814	AU 1980-54763	19800121
AU 528592	B2	19830505		
ZA 8000371	A	19810325	ZA 1980-371	19800122
GB 2043245	A	19801001	GB 1980-2743	19800128
GB 2043245	B2	19830525		
SE 8000843	A	19800806	SE 1980-843	19800201
SE 448259	B	19870202		
SE 448259	C	19870514		
JP 55104896	A2	19800811	JP 1980-10117	19800201
AT 8000560	A	19810615	AT 1980-560	19800201
AT 365781	B	19820210		
NL 8000698	A	19800807	NL 1980-698	19800204
FR 2447966	A1	19800829	FR 1980-2385	19800204
FR 2447966	B1	19841019		
ES 488263	A1	19801216	ES 1980-488263	19800204
CH 641569	A	19840229	CH 1980-877	19800204
BE 881557	A1	19800805	BE 1980-199272	19800205
US 4550163	A	19851029	US 1981-228414	19810126

PRIORITY APPLN. INFO.: US 1979-9007 19790205

AB An enzyme inhibition immunoassay was developed based on the competitive binding of an antibody to either an antigen (the substance whose quantity is unknown) or a ligand-bound enzyme inhibitor (which will be inactivated when reacted with the antibody. The ligand has structural similarities to the antigen, and the enzyme inhibitor will inactivate the enzyme whose activity is being measured, unless free antibody has reacted with the ligand-inhibitor complex. Therefore, enzyme activity is inversely related to antigen concn. Thus, for the detn. of serum digoxin, to 50-.mu.L serum samples contg. 0.1-1.30 .mu.M digoxin were added antidigoxin antibodies, N-ethylmaleimide (NEM), compd. I (a digoxin analog-acetylcholinesterase inhibitor conjugate), and N-methylorphenadrine, which is an inhibitor of human serum acetylcholinesterase but not of the indicator acetylcholinesterase of Electrophorus electricus, which is used in the assay. The final concns. were: antibody 8.0 .times. 10-7M, NEM 1.6 mM, compd. I 4.5 .times. 10-7M, and N-methylorphenadrine .apprx.1 mM. The complete solns. were incubated 12 min, and acetylcholinesterase of E. electricus was added to each. After 26 min, an aliquot of each sample was dild. 26 fold with test buffer (0.1 M phosphate-gelatin, pH 7.0) contg. 5 .times. 10-4M acetyl-.beta.-methylthiocholine iodide as substrate, 1.6 .times. 10-5M 5,5'-dithiobis(2-nitrobenzoate) (which reacts with the product of the enzyme reaction, thiocholine), and 1 mM

L6 ANSWER 35 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
N-methylorphenadrine. The final enzyme concn. was .apprx.2 .times. 10-12M, and the reaction solns. were analyzed spectrometrically at 412 nm after 5-min incubation at 30.degree.. The absorbance changes were inversely related to digoxin concn.

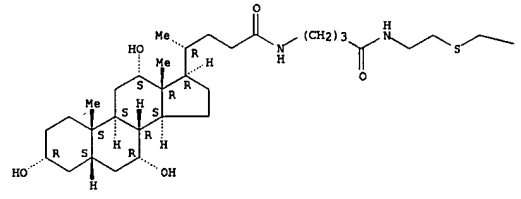
IT **75897-32-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for enzyme inhibition immunoassay)

RN 75897-32-4 CAPLUS

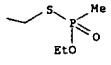
CN Cholan-24-amide, 3,7,12-trihydroxy-N-(12-methyl-12-oxido-4-oxo-13-oxa-8,11-dithia-5-aza-12-phosphapentadec-1-yl)-, (3.alpha.,5.beta.,7.alpha.,12.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



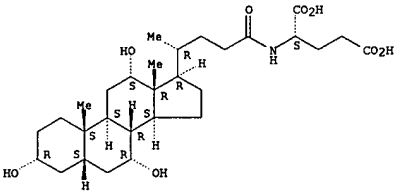
PAGE 1-B



RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, in glycocholate detn. by enzyme inhibition immunoassay

L6 ANSWER 36 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1980:215738 CAPLUS
DOCUMENT NUMBER: 92:215738
TITLE: Bile acid derivatives with antimicrobial activity
AUTHOR(S): Bellini, A. M.; Vertuani, G.; Quaglio, M. P.; Cavazzini, G.
CORPORATE SOURCE: Ist. Chim. Farm. Tossicol., Univ. Ferrara, Ferrara, Italy
SOURCE: Farmaco, Edizione Scientifica (1979), 34(11), 967-78
CODEN: FRPSAX; ISSN: 0430-0920
DOCUMENT TYPE: Journal
LANGUAGE: Italian
AB Bile acid amino acid I and II (X = Ala, Ser, Glu, NHCH(CH2CH2NH2)CO, Orn) and I (X = Arg) were prepd. in 60-80% yield by the mixed anhydride or active ester methods. I and II were bactericidal against both gram-pos. and gram-neg. bacteria.
IT **73386-10-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and bactericidal activity of)
RN 73386-10-4 CAPLUS
CN L-Glutamic acid, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

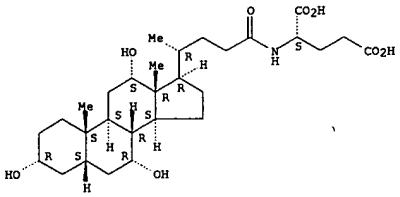


● Na

IT **23828-78-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 23828-78-6 CAPLUS
CN L-Glutamic acid, N-[(3.alpha.,5.alpha.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

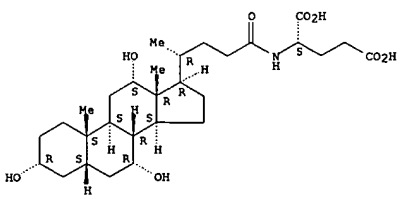
Absolute stereochemistry.

L6 ANSWER 36 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



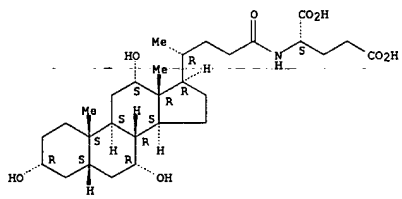
L6 ANSWER 37 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1975:30035 CAPLUS
DOCUMENT NUMBER: 82:30035
TITLE: Influence of synthetic conjugates of cholic acid on cholesteremia in rats
AUTHOR(S): Story, Jon A.; Tepper, Shirley A.; Kritchevsky, David
CORPORATE SOURCE: Wistar Inst. Anat. Biol., Philadelphia, PA, USA
SOURCE: Journal of Nutrition (1974), 104(9), 1185-8
CODEN: JONUAI; ISSN: 0022-3166
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects on serum and liver cholesterol levels in rats of 2 naturally occurring conjugates of cholic acid (taurocholic and glycocholic acids) and 4 synthetic conjugates (glutamocholic, aspartocholic, cysteocholic, and cysteinocholic acids) (0.5% diet), in combination with cholesterol (0.5% of diet) were investigated. Hydrolysis of these conjugates by cholylglycine hydrolase (EC 3.5) was was also measured. Cholesterol alone did not cause cholesteremia but when fed with cholic acid or any of its conjugates, except aspartocholate, the animals had significantly higher serum-liver cholesterol pools (15-70%). The aspartocholic acid-fed group had serum and liver cholesterol levels significantly lower than the cholic acid:cholesterol-fed animals but similar to control animals. When the degree of hydrolysis of each of the conjugates by cholylglycine hydrolase was measured, all conjugates were hydrolyzed to a similar extent (77-87%) except aspartocholic (36%) and cysteinocholic acids (42%). Apparently there is a realtion between the ability of a cholic acid conjugate to produce elevated serum and(or) liver cholesterol levels in rats and the degree to which it is hydrolyzed by the intestinal microflora.
IT **23828-78-6**
RL: BIOL (Biological study)
(cholesteremia in relation to dietary)
RN 23828-78-6 CAPLUS
CN L-Glutamic acid, N-[(3.alpha.,5.alpha.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 38 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1971:415115 CAPLUS
DOCUMENT NUMBER: 75:15115
TITLE: Mechanism of removal of histones from chromatin by deoxycholate
AUTHOR(S): Hadler, Stephen C.; Smart, John E.; Bonner, James
CORPORATE SOURCE: Div. Biol., California Inst. Technol., Pasadena, CA, USA
SOURCE: Biochimica et Biophysica Acta (1971), 236(1), 253-8
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Effects of several cholanic acids and their conjugated derivs. on the selective dissocn. of slightly lysine-rich histones II from chromatin were studied. The driving force for the interaction between the cholanic acid anion and histones seems to be the lowering of the activity coeff. of the cholanic acid anion which occurs when it is partially removed from soln. by interaction with hydrophobic regions of the pos. charged histones. The complete sepn. of chromatin and 14C-labeled Na deoxycholate by sucrose sedimentation indicated that the binding of Na deoxycholate to chromatin is readily and completely reversible.
IT **32795-01-0**
RL: BIOL (Biological study)
(histone removal from chromatin by)
RN 32795-01-0 CAPLUS
CN L-Glutamic acid, N-[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]-, sodium salt (9CI) (CA INDEX NAME)

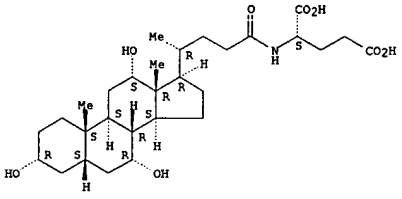
Absolute stereochemistry.



●x Na

L6 ANSWER 39 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1970:119954 CAPLUS
DOCUMENT NUMBER: 72:119954
TITLE: Effects of N-cholyl and N-dehydrocholylamino acids on the experimental liver injuries
AUTHOR(S): Kaneko, Hidehiko; Kadokawa, Toshiaki; Aonuma, Shigeru
CORPORATE SOURCE: Res. Lab., Dainippon Pharm. Co., Ltd., Osaka, Japan
SOURCE: Yakugaku Zasshi (1970), 90(2), 169-75
CODEN: YKKZAJ; ISSN: 0031-6903
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Effects of N-cholyl and N-dehydrocholylamino acids on CCl4 liver injury in rabbits were examd. Dehydrocholylmethionine and its Et ester exhibited a protective effect against this injury. These compds. were protective against fatty infiltration of the liver induced by CCl4, ethionamide, and EtOH. The mode of action of these protective agents is discussed.
IT **23828-78-6**
RL: BIOL (Biological study)
(fatty liver prevention by)
RN 23828-78-6 CAPLUS
CN L-Glutamic acid, N-[(3.alpha.,5.alpha.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

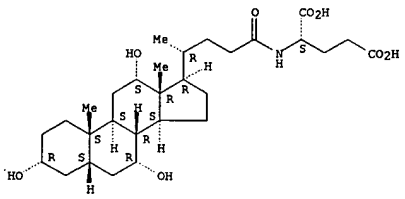


L6 ANSWER 40 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1969:491870 CAPLUS
DOCUMENT NUMBER: 71:91870
TITLE: Cholyl-.alpha.-amino acids
INVENTOR(S): Aonuma, Shigeru; Kaneko, Hidehiko
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co., Ltd.
SOURCE: Jpn. Tokkyo Koho, 3 pp.
CODEN: JAXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 44016891	B4	19690725	JP	19651026

AB Cholic acid (4.1 g.) is dissolved in a mixt. of 2.4 ml. NBu3 and 20 ml. dioxane, 1 ml. Et chlorocarbonate added at 10.degree., the mixt. added to 20 ml. N NaOH contg. 1.8 g. L-tyrosine, stirred 30 min., concd. in vacuo, the residue dissolved in H2O, and the soln. acidified with HCl to give 4.2 g. cholyl-L-tyrosine, m. 232.degree. (dil. EtOH). Similarly prepd. are choly-L-leucine, m. 114.degree. (decompn.), and choly-L-glutamic acid, m. 98.degree. (decompn.). The products lower the concn. of cholesterol in blood.
IT **23828-78-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 23828-78-6 CAPLUS
CN L-Glutamic acid, N-[(3.alpha.,5.alpha.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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